VOLUME 49 NUMBER 1 JANUARY, 1960

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

CONTENTS

DEPARTMENTS

For a complete table of contents see page xlv

Publication office: Curtis Reed Plaza, Menasha, Wisconsin

Copyright, 1960, Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois

Subscription price in United States twelve dollars yearly. In Canada and foreign countries fourteen dollars. Published monthly by the Ophthalmic Publishing Company. Subscription and Advertising Office: 664 North Michigan Avenue, Chicago 11, Illinois. Entered as second class matter at the post office at Menasha, Wisconsin. Printed in U.S.A.

Eyes Made To Order

Walter Melcher is applying color on an artificial eye. He needs the skill of an expert glass blower plus the coloring technique of an artist to match eyes of all shapes and colorings. Fortunately, Walter is heir to 105 years' experience. Our skilled glass and plastic eyemakers have passed along and perfected their technics since 1851. These men visit most areas regularly to make artificial eyes that are perfectly matched for your patients—another reason to call or write our nearest office on your next replacement.

Complete Artificial Eye Service

- Eyes custom made—glass or plastic
- Eyes from stock sent on memorandum same day order received—glass or plastic
- Damaged or broken artificial eyes accurately matched
- Fitted to all types of motility implants
- Implants, X-Ray therapy shields, foreign body locators
- Superior Quality—Finest Workmanship

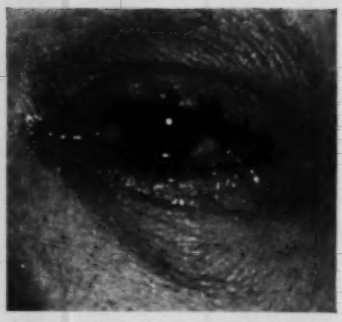
Serving the Profession Since 1851

Mager and Gougelman inc.

30 North Michigan Avenue, Chicago 2, Illinois : 120 E. 56th St., New York 22, New York

DETROIT • CLEVELAND • KANSAS CITY • MINNEAPOLIS • ST. LOUIS
HOUSTON (Soper Bros.) • BOSTON • PHILADELPHIA • PITTSBURGH • WASHINGTON

"The eyes were grossly inflamed, infection was present and the patient was uncomfortable, unsightly and disturbed over appearance and condition. Over a period of more than 12 months the patient had received at least six different topical preparations—with little or no benefit...."[1]



Miss U. L.: 6/12

Miss U. L.: 7/10

"...On 6/12 started Predmycin—one drop in each eye every half hour until inflammation had subsided markedly (approx. 72 hours) then reduced dosage intervals to every 3 hours while awake. At visit 7/10, patient was completely symptom-free. She expressed considerable gratefulness for the early subjective relief and short clinical course."[1]

Predmycin®

Ophthalmic Solution

An ideal solution for ocular inflammation complicated by infection

Predmycin affords simultaneous antimicrobial and anti-inflammatory action for rapid control of infectious and potentially infectious anterior segment eye disorders. Predmycin's formulation provides a threefold therapeutic approach that quickly improves the eye's appearance, effectively and safely attacks the pathogen and counteracts the inflammatory process:

- *Prednisolone alcohol 0.2%*—potent anti-inflammatory agent[2]—checks inflammation preserving the functional integrity of the eye and relieves pain, often within a few hours. In vitro studies indicate that prednisolone alcohol greatly increases neomycin's antibacterial potency.[3]
- *Neomycin sulfate 0.5%*—one of the most potent and least sensitizing topical antibiotics, attacks over 90% of the bacteria causing infection of the eye's anterior segment.[4] Studies indicate Predmycin's corticosteroid greatly potentiates the antibacterial action of neomycin against Staph. aureus and Strep. hemolyticus.[3]
- *Phenylephrine HCl 0.12%*—the preferred ocular decongestant—rapidly improves the eye's appearance, allays irritation and localizes the prednisolone in the tissues.[4]

PREDMYCIN—for optimal control of infectious, inflammatory and allergic conditions of the eyelids, conjunctiva, cornea, sclera, uveal tract. Dosage: 1 to 2 drops in the eyes, two to four times a day. Predmycin does not sting or burn. Supplied: 5 cc. plastic dropper bottles—on prescription only.

References: 1. Gordon, D. M.: Personal communication. 2. deRoeth, A., Jr.: A.M.A. Arch Ophth. *324*:62 (Aug. 1) 1959. 3. Wilkins, J. R.: Antibiotics & Chemotherapy *9*:464 (Aug.) 1959. 4. Gordon, D. M.: Am. J. Ophth. *47*:536 (April) 1959.

Photographs courtesy of Dr. Dan M. Gordon, New York Hospital - Cornell Medical Center, New York.

ALLERGAN CORPORATION, *Los Angeles 17, California*

CYCLOBAR™ sterile ophthalmic gel

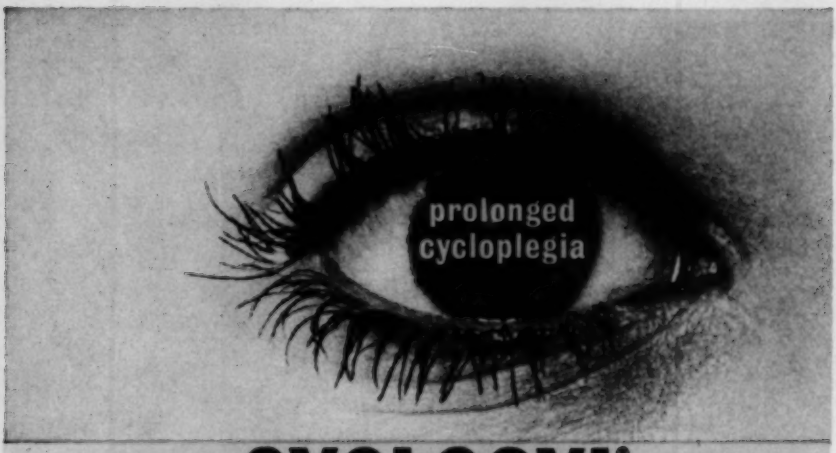
(CYCLOGYL® HCl 1.0% [cyclopentolate hydrochloride, Schieffelin], methylcellulose, and neomycin citrate 0.55%.)

Fast-acting cycloplegic and mydriatic agent[1] plus the potent antibiotic action of neomycin—"...effective against [a wide] range of organisms met in ocular infections...."[2] Unexcelled for pre- and post-operative therapy, infectious disorders and injured eyes. Holds the pupil in an open, relaxed position ...controls infection...helps prevent adhesions... relieves inflammation. Long-acting CYCLOBAR can't be blinked out. When desired, miotics will return the eye to normal within 6 hours;[3] without miotics, the eye will return to normal in 24 hours.[4] No evidence of irritation or sensitization has been reported.

References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Sorsby, A.: Ann. Roy. Coll. Surgeons of England *22*:107, 1958. 3. Costner, A. N.: South. M. J. *48*:1192, 1955. 4. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955.

Supplied in collapsible tubes of 3.54 Gm.
Samples and literature available on request.

Schieffelin & Co. / Since 1794
PHARMACEUTICAL LABORATORIES DIVISION, New York 3, N. Y.



new CYCLOGYL® gel

Prompt, complete cycloplegia in new, long-acting gel form. Can't be blinked out, so its action is concentrated and prolonged. Can be used in conjunction with topical steroid or antibiotic therapy.

CYCLOGYL® FOR ALL-PURPOSE CYCLOPLEGIA

"...Acts so quickly and wears off so quickly that loss of time for doctor and patient is minimal."[1] Recovery within 6 hours or less with a miotic[2]...within 24 hours without.[3] Unexcelled for refraction...valuable for treatment of lesions, inflammatory conditions and pre- and postoperative therapy. No toxic or allergic reactions reported[4]...well-tolerated by children and elderly patients.[1,3]

CYCLOGYL® Gel
Sterile ophthalmic gel. (CYCLOGYL HCl 1.0% in a neutral gel, Schieffelin.)

CYCLOGYL®
Sterile ophthalmic solution. (cyclopentolate hydrochloride, Schieffelin.)

Supplied:
Dark-pigmented iris—2.0% solution with PVP (polyvinylpyrrolidone). 7.5 ml. and 2 ml. dropper bottles.
Brown or hazel iris—1.0% solution. 15 ml. and 2 ml. dropper bottles.
Blue, gray and green iris—0.5% solution. 15 ml. dropper bottles.
Prolonged therapy—Gel. 3.54 Gm. collapsible tubes.
Samples and literature supplied on request.

References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Costner, A. N.: South. M. J. *48*:1192, 1955. 3. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955. 4. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. *38*:831, 1954.

Schieffelin & Co. / Since 1794
PHARMACEUTICAL LABORATORIES DIVISION, New York 3, N. Y.

"the fastest-acting mydriatic"[1]

FOR
MYDRIASIS

Rapid, profound mydriasis[1,2] with minimal cycloplegia... even in heavily pigmented irises. Excellent for ophthalmoscopic observation... resists the counteracting effects of bright lights. Quick return to normal—within 6 hours with a miotic,[3] within 24 hours without a miotic.[4] No evidence of side effects[5]... well-tolerated by children and elderly patients.[1,4]

CYCLOMYDRIL®

(CYCLOGYL® HCl 0.2% [cyclopentolate hydrochloride, Schieffelin], and phenylephrine hydrochloride 1.0% with PVP [polyvinylpyrrolidone] 3.0% in a sterile ophthalmic solution.)

Supplied in 7.5 ml. and 2 ml. dropper bottles.

Samples and literature available on request.

References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Priestly, B. S.; Medine, M. M., and Phillips, C. C.: to be published. 3. Costner, A. N.: South. M. J. *48*:1192, 1955. 4. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955. 5. New and Nonofficial Drugs: J. B. Lippincott Company, 1958, p. 243.

Schieffelin & Co./Since 1794

PHARMACEUTICAL LABORATORIES DIVISION • New York 3

LEDERLE INTRODUCES...

a masterpiece

greater antibiotic activity

Milligram for milligram, DECLOMYCIN brand of Demethylchlortetracycline has 2 to 4 times the inhibitory capacity of tetracycline against susceptible organisms. (*Activity* level is the basis of comparison—not quantitative blood levels—since action upon pathogens is the ultimate value.*) Provides significantly higher serum activity level . . .

with far less antibiotic intake

DECLOMYCIN demonstrates the highest ratio of prolonged activity level to daily milligram intake of any known broad-spectrum antibiotic. Reduction of antibiotic intake reduces likelihood of adverse effect on intestinal mucosa or interaction with contents.

unrelenting-peak antimicrobial attack

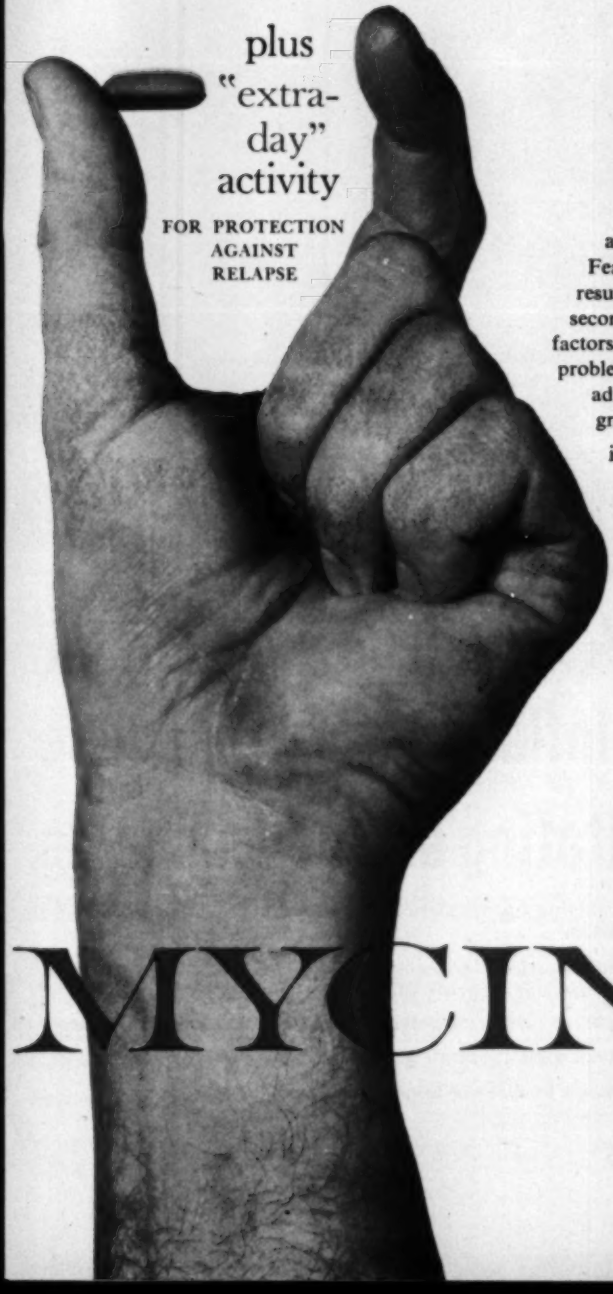
The DECLOMYCIN high activity level is uniquely constant throughout therapy. Eliminates peak-and-valley fluctuation, favoring continuous suppression. Achieved through remarkably greater stability in body fluids, resistance to degradation, and a low rate of renal clearance.

*Hirsch, H. A., and Finland, M.: *New England J. Med.* 260:1099 (May 28) 1959.

DECLO

Demethylchlortetracycline Lederle

# of antibiotic design



plus "extra-day" activity

FOR PROTECTION AGAINST RELAPSE

DECLOMYCIN maintains activity for one to two days after discontinuance of dosage. Features unusual security against resurgence of primary infection or secondary bacterial invasion—two factors often resembling a "resistance problem"—enhancing the traditional advantages of tetracycline... for greater physician-patient benefit

in the distinctive, dry-filled, duotone capsule

immediately available as:

DECLOMYCIN Capsules, 150 mg., bottles of 16 and 100. Adult dosage: 1 capsule four times daily.

DECLOMYCIN Pediatric Drops, 60 mg. per cc., 10 cc. bottles with dropper.

DECLOMYCIN Oral Suspension, 75 mg. per 5 cc. tsp.

MYCIN®

Lederle

LEDERLE LABORATORIES
a Division of
AMERICAN CYANAMID COMPANY
Pearl River, New York

Acute conjunctivitis[1] before treatment, showing engorged irregular superficial vessels

NOW...the true solution for fast anti-inflammatory response and no irritating steroid particles

- mg. for mg. the most active steroid topically—up to 40 times the potency of hydrocortisone
- optimal not minimal steroid concentration in true solution for peak effectiveness . . . maximal contact at the site of the lesion
- quick-acting broad antimicrobial activity when infection threatens recovery
- superior patient comfort—no stinging, no irritating particles, bland carrier

1. Gordon, D. M.: Scientific Exhibit, American Medical Association, Annual Meeting, San Francisco, 1958.

4 days after treatment ACTUAL CLINICAL PHOTOGRAPHS

OPHTHALMIC SOLUTION

NeoDecadron*

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

INDICATIONS: Trauma—mechanical, chemical or thermal; conjunctival, corneal, or uveal tract inflammation involving the anterior segment; allergy; blepharitis.

DOSAGE: NeoDECADRON Ophthalmic Solution (0.1%)—One drop 4-6 times daily.
NeoDECADRON Ophthalmic Ointment (0.05%)—Applied 3-4 times daily.

In severe or sight-threatening conditions, the frequency of administration may be increased. Systemic therapy with DECADRON Tablets may be prescribed adjunctively.

PRECAUTION: Steroid therapy should never be employed in the presence of tuberculosis or herpes simplex.

Additional information is available to physicians on request.

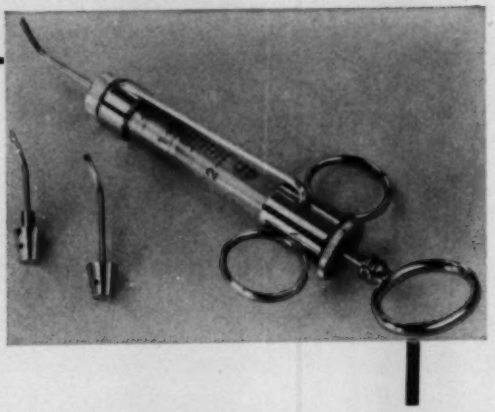
*NeoDECADRON and DECADRON are trademarks of Merck & Co., Inc.

Product	Steroid Concentration	active ingredients: Dexamethasone 21-Phosphate (as the disodium salt)	active ingredients: Neomycin Sulfate	Supplied
NeoDECADRON Ophthalmic Solution	0.1%	1 mg./cc.	5 mg./cc. (equivalent to 3.5 mg. neomycin base)	5 cc. (¼ oz.) sterile dropper-bottles
DECADRON Phosphate Ophthalmic Solution	0.1%	1 mg./cc.	—	5 cc. (¼ oz.) sterile dropper-bottles
NeoDECADRON Ophthalmic Ointment	0.05%	0.5 mg./Gm.	5 mg./Gm. (equivalent to 3.5 mg. neomycin base)	3.5 Gm. (⅛ oz.) tubes
DECADRON Phosphate Ophthalmic Ointment	0.05%	0.5 mg./Gm.	—	3.5 Gm. (⅛ oz.) tubes

MSD MERCK SHARP & DOHME
Division of Merck & Co., Inc. • Philadelphia 1, Pa.

storz
Surgical Instruments

Syringe
Two-Way
J. FUCHS, M.D.



For Use in the Removal of Lens Residue and Substance, Irrigation Following Hemorrhage, and in Conjunction with Removal of Soft, Traumatic or Congenital Cataracts

E-4882 Syringe, Two-way, FUCHS: with two side opening canulas, one each E-4885 and E-4886. Designed by Dr. Fuchs of Stuttgart, Germany, and introduced in the United States at the International Congress of Ophthalmology, New York, 1954. Presented at the 1958 Meeting of the American Academy of Ophthalmology and Otolaryngology by Dr. Louis Daily.

The two-way syringe with double canulas supplies simultaneous irrigation and aspiration. The fluid in the anterior chamber can be changed several times with one motion and without varying the volume of the anterior chamber. This fluid introduction and simultaneous removal causes a swirling action within the anterior chamber. As the piston moves downward within the barrel of the syringe the fluid is forced from one of the double canulas. At the same time the upper part of the barrel, being vacated by the downward moving piston, creates a vacuum which causes the fluid within the anterior chamber to be drawn into the second of the canulas which is connected by a tube to the upper chamber of the syringe.

$95.00

E-4883 Syringe, Two-way, FUCHS: with 3 canulas, one each E-4885, E-4886 side opening, and one E-4887 end opening canula. $110.00

E-4885 Extra Canula: Side opening, 1.4 mm $19.50

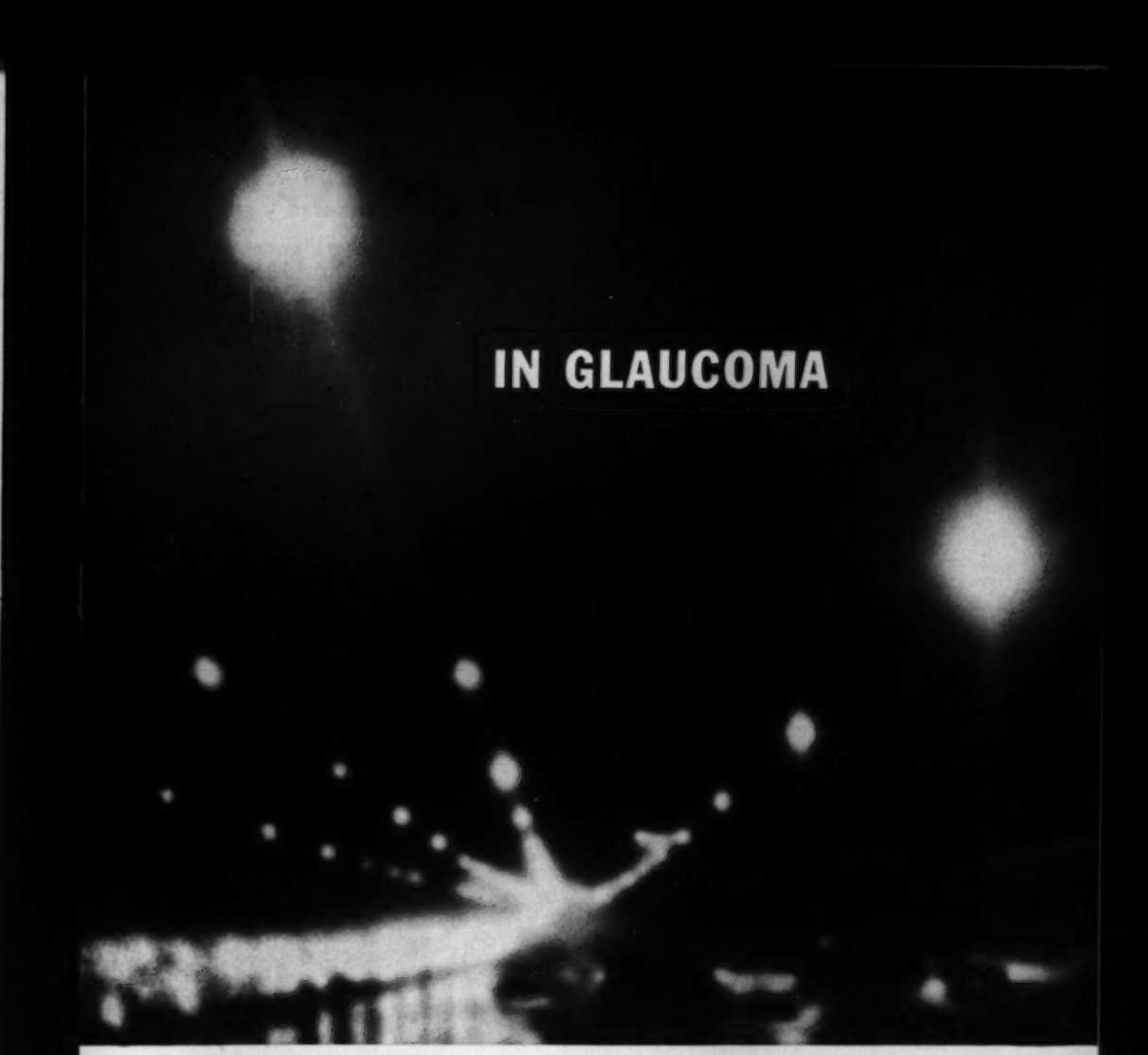
E-4886 Extra Canula: Side opening, 1.6 mm $21.50

E-4887 Extra Canula: End opening, 1.6 mm $21.50

Instructions for maintenance cleaning, assembly and sterilization supplied with each instrument

STORZ INSTRUMENT COMPANY • 4570 Audubon Avenue, St. Louis 10, Missouri

New York Showroom: 157 E. 64th St. at Lexington Ave.



All Alcon Miotics have these product advantages: a Methylcellulose vehicle (which is chemically inert) to provide prolonged contact, give unexcelled absorption of drugs, lubricate and soothe the eye . . . strict quality control to assure sterility and uniform potency from bottle to bottle . . . tonicity and pH adjustments to give optimum patient comfort with maximum therapeutic effectiveness . . . sterile 15 cc. Drop-Tainer® packaging which reduces the likelihood of contamination during use . . . preservatives added.

Alcon Miotics have GREEN caps and dropper tips for easy identification.

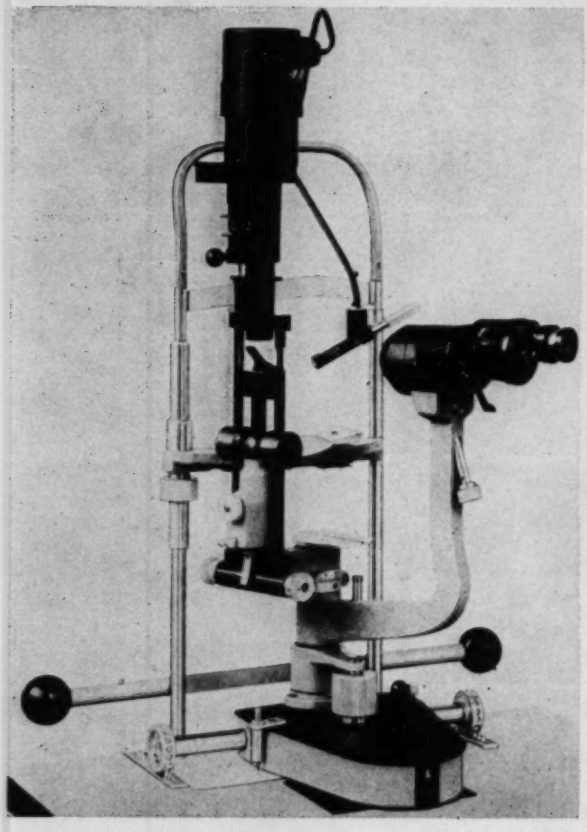
each a product of choice

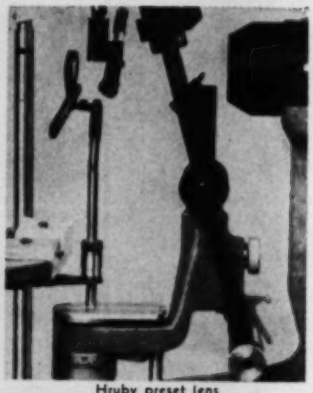
- **ISOPTO® CARBACHOL**—Carbachol U.S.P. in three concentrations (0.75%, 1.5% and 3%) in a 1% Methylcellulose vehicle.
- **ISOPTO® CARPINE**—Pilocarpine HCl U.S.P. in six concentrations (0.25%, 0.5%, 1%, 2%, 3% and 4%) with 0.5% Methylcellulose.
- **ISOPTO® P-ES**—Pilocarpine HCl U.S.P. (2%), Eserine Salicylate U.S.P. (0.25%) in a 0.5% Methylcellulose vehicle.
- **ISOPTO® ESERINE**—Eserine Salicylate U.S.P. in two concentrations (0.25% or 0.5%) in a 0.5% Methylcellulose vehicle.

Available at prescription pharmacies throughout the United States and Canada

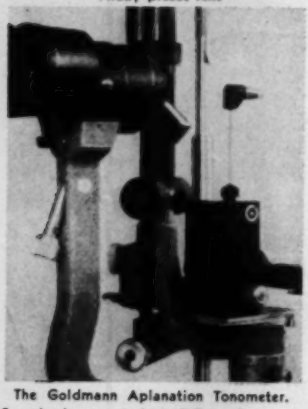
Alcon **ALCON LABORATORIES, INC., FORT WORTH, TEXAS**

THE ALL NEW HAAG STREIT SLIT LAMP "900"





Hruby preset lens



The Goldmann Aplanation Tonometer.
Can also be mounted on all Zeiss slit lamps.

"This slit lamp is the answer to every Ophthalmologist's dream . . ." or "I am running out of superlatives to describe this slit lamp . . ." These and similar statements were made by leading Ophthalmologists when they viewed the first models of this all new instrument. Amongst many other features, here are a few of its outstanding ones:

Oblique, horizontal and vertical optical sections
Illumination is up to 2× brighter than in present model
Extremely convenient arrangement of all controls
Fixation light eliminates accommodation and convergence of patient
Unexcelled finish and Swiss precision workmanship

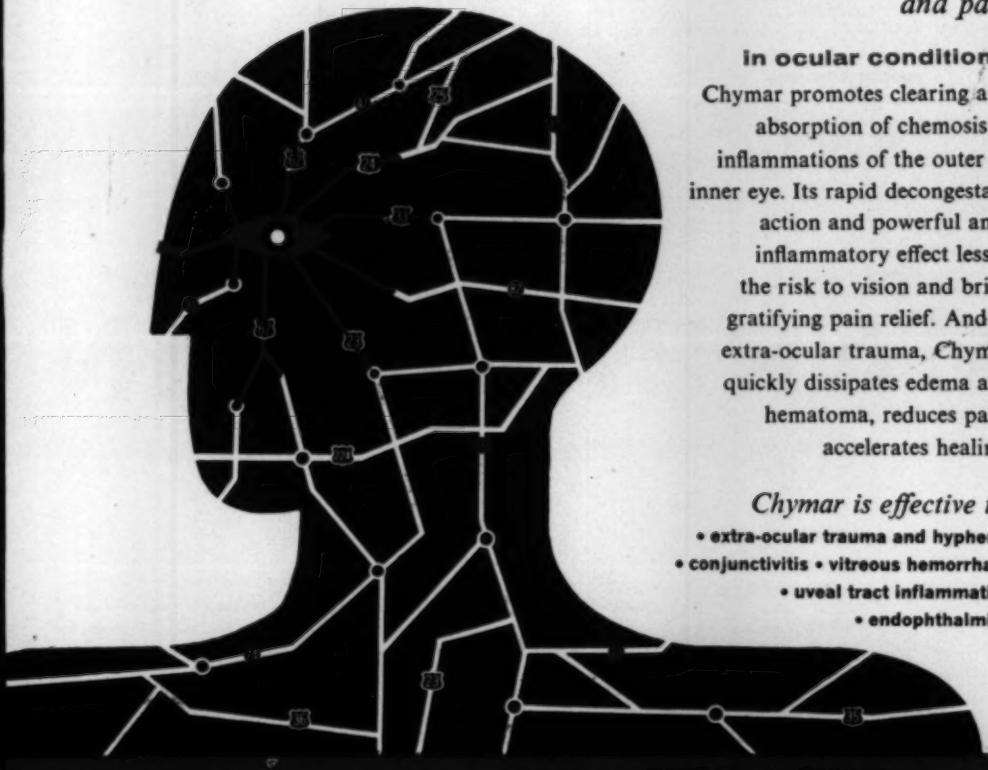
Brochures are available on request

ALFRED P. POLL

Ophthalmological Instruments of Top Quality

40 West 55th Street **New York 19, N.Y.**

systemic route to faster healing



controls inflammation, swelling and pain

in ocular conditions

Chymar promotes clearing and absorption of chemosis in inflammations of the outer or inner eye. Its rapid decongestant action and powerful anti-inflammatory effect lessen the risk to vision and bring gratifying pain relief. And in extra-ocular trauma, Chymar quickly dissipates edema and hematoma, reduces pain, accelerates healing,

Chymar is effective in:

- **extra-ocular trauma and hyphema**
- **conjunctivitis**
- **vitreous hemorrhage**
- **uveal tract inflammation**
- **endophthalmitis**

CHYMAR®

superior anti-inflammatory enzyme

Buccal / Aqueous / Oil

CHYMAR *Buccal*
Crystallized chymotrypsin in a tablet formulated for buccal absorption. Bottles of 24 tablets. Enzymatic activity, 10,000 Armour Units per tablet.

CHYMAR *Aqueous*
Solution of crystallized chymotrypsin in sodium chloride injection for intramuscular use. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

CHYMAR
Suspension of crystallized chymotrypsin in oil for intramuscular injection. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

and for enzymatic sterile lysis. Also CHYMAR

ARMOUR PHARMACEUTICAL COMPANY

FOR POTENT MIOSIS

. . . in chronic non-congestive glaucoma

CARBAMIOTIN

CAREACHOL U. S. P.

Iso-Sol brand of sterile, dated, low surface tension solution of Carbamylcholine Chloride with Benzalkonium Chloride 1:10,000 as the wetting agent.

¾% and 1½%

ADVANTAGES

Acts indirectly by inhibiting cholinesterase and permits natural acetylcholine to act without interference . . . not susceptible to destruction by cholinesterase . . . low allergic index . . . prolonged use will not produce synechia . . . lasts longer — less frequent administration . . .

INDICATIONS

For reduction of intraocular tension in chronic, non-congestive glaucoma . . . can replace pilocarpine or eserine in manifestations of allergy, sensitization or lack of response to these drugs . . .

PACKAGING

In 15cc. sterile sealed Lacrivials® ¾% and 1½%

For samples, literature and bibliography, write . . .

ISO-SOL®

THE ISO-SOL COMPANY, INC.
LINDENHURST, N. Y.

Pioneer Specialists in Sterile Ophthalmic Solutions

dynamic control of GLAUCOMA

IN DIAGNOSIS – By reducing corneal edema, DIAMOX facilitates examination and diagnosis in ophthalmologic disorders.

AS THERAPY – By lowering intraocular pressure, conservative therapy with DIAMOX can often reduce the need of surgical intervention in various glaucomatous conditions. Traumatic hyphemas, for example, can be resolved without cyclodiathermy puncture.[1]

PRE- AND POSTOPERATIVE CARE – Where surgery is required, tension is first reduced by DIAMOX and maintained after surgery to speed healing. Used with miotics, the synergistic action improves efficacy.[1]

Suggested DIAMOX dosage for glaucoma: 250 mg. every four hours. In severe glaucomatous crises, the intravenous form may provide quicker reduction of global pressure.

Supplied: Scored tablets of 250 mg., and Vials of 500 mg. for parenteral use.

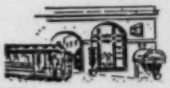
1. Venable, H. P.: J. Nat. M. A., 50:79, 1958.

DIAMOX

HCO_3 regulating diuretic

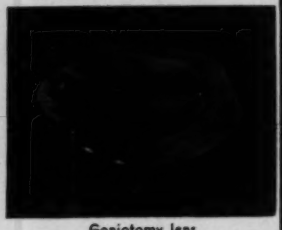
Acetazolamide Lederle

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York



Equipment for GONIOSCOPY and GONIOTOMY after Otto Barkan, M.D.

Koeppe Diagnostic lens #6165

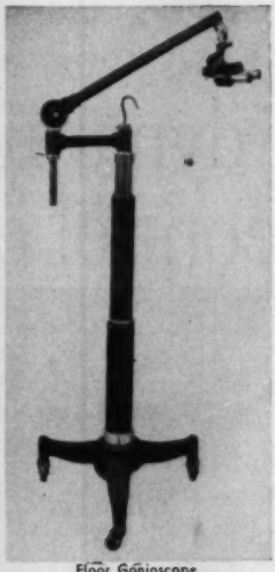


Goniotomy lens #6180

Operating Lamp on Stand #6140

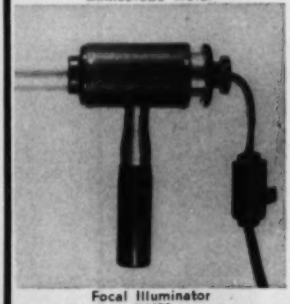
6100	Gonioscope (floor)*	$390.00
6101	Stand only*	195.00
6110	Haag-Streit microscope, single power, 15×	195.00
6120	Haag-Streit microscope, two power, 10×-20×	250.00
	Charge for fitting your scope to 6101 stand	10.00
6127	Haag-Streit microscope with handle, 15×	195.00
6150	Otto Barkan Focal Illuminator with plug-in transformer*	47.50
6165	Otto Barkan Koeppe diagnostic lens, three sizes: 16-18-20 mm. lip diameters*	45.00
6175	Otto Barkan Goniotomy lens (surgical) Infant size*	45.00
6180	Otto Barkan Goniotomy lens (surgical) child-adult size*	45.00
6130	Otto Barkan operating lamp, hand model*	72.50
6140	Otto Barkan operating lamp, floor model*	97.50
6191	Otto Barkan Goniotomy knife (selected model)*	9.75

** Manufactured exclusively by Parsons Optical Laboratories.*



Floor Gonioscope #6100

Haag-Streit Hand Microscope for Gonioscope #6127



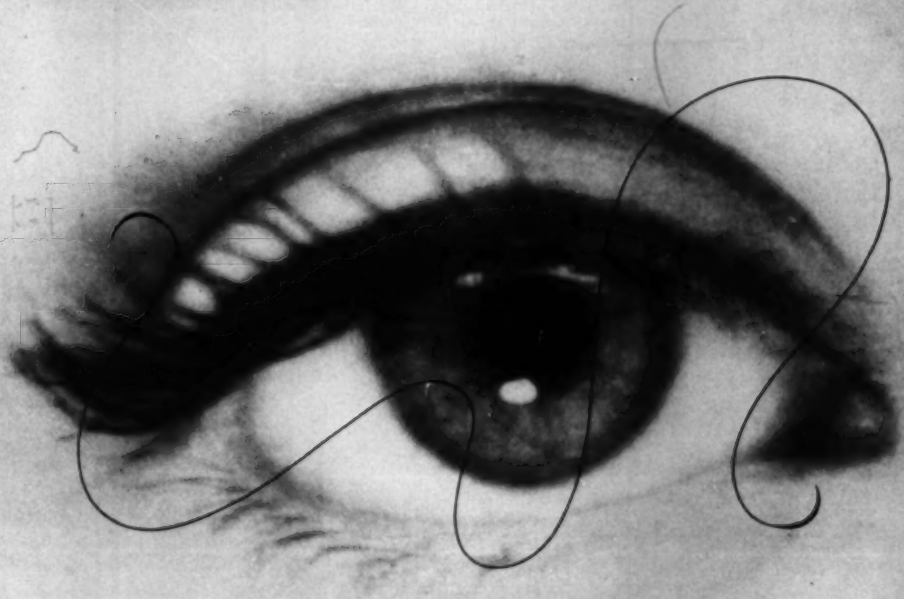
Focal Illuminator #6150

PARSONS OPTICAL LABORATORIES

518 POWELL STREET · SAN FRANCISCO 2, CALIFORNIA

DESIGNED FOR YOUR MOST EXACTING REQUIREMENTS

ETHICON® OPHTHALMIC NEEDLE SUTURES



- hand-finished Micro-Point® needles
- unequaled sharpness by hand honing
- 40% greater strength
- increased stability in needle holder
- reduced tendency to cut out of tissue

ETHICON EYE SUTURES with Tru-Tempered reverse cutting needles for maximum strength and minimum tendency to cut out of tissue.

ETHICON®

MINIM-IZE

oxidation ■ decomposition ■ color change ■ wastage of ophthalmic drugs

...with the revolutionary new concept of sterile single-dosage unit packaging: **MINIMS®**

Ophthalmic drugs packaged as MINIMS are conveniently available for use without the need for worry about the irritation, stinging, or chemical changes sometimes caused by exposure to atmosphere.

The sterile single-patient dispenser is encased in a sterile plastic film outer wrap. Your nurse tears open the outer wrap, snips off the end of the MINIMS unit, administers the drug, throws the used unit away.

Example of Advantages: Eserine packed in MINIMS units subjected to laboratory tests maintained its potency well over two years—without the formation of rubreserine and with no irritation upon instillation. Furnished as Eserine Salicylate 0.25% and 0.5.

MINIMS UNITS CONTAIN SUFFICIENT VOLUME FOR SINGLE-PATIENT EXAMINATION.

Also Available: 20-unit packs of MINIMS containing the following drugs: Atropine Sulfate 1% and 2% • Homatropine Hydrobromide 2% and 5% • Phenylephrine Hydrochloride 2.5% and 10% • Pilocarpine Nitrate 1% and 2% • Scopolamine Hydrobromide 0.2% • Tetracaine Hydrochloride 0.5%

Manufactured by
BARNES-HIND Ophthalmic Products, Inc., 895 Kifer Road, Sunnyvale, California, REgent 6-5462

OPHTHOCORT® IN EYE INFECTIONS

"...is effective against most gram-positive and gram-negative cocci and some gram-negative bacilli. It rarely produces dermatitis and resistant strains are uncommon."[1] "...penetrates the noninflamed eye better than any other antibiotic, regardless of route of administration."[2]

"...gram-negative bacilli are being isolated with increasing frequency from the conjunctiva...."[3] Polymyxin B "...is bactericidal against most gram-negative microorganisms...."[4]

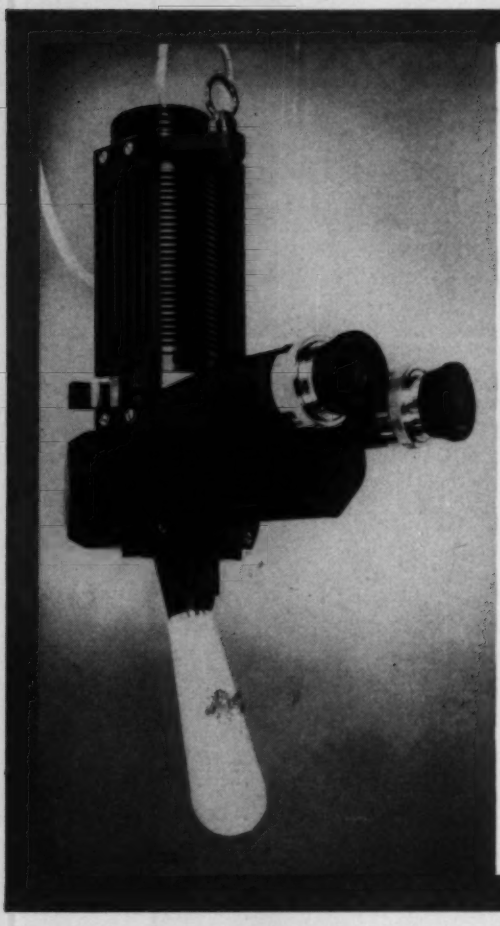
"Cortisone, hydrocortisone and ACTH, by altering the inflammatory responses of the body, cause a decreased amount of scarring and vascularization."[5] "Hydrocortisone is about twice as potent gram for gram as cortisone, even when given locally."[5]

Provides wide-spectrum antibacterial, anti-inflammatory, and antiallergic action for topical treatment of patients with ocular inflammation complicated by infection.

Local application two to four times daily as required.

OPHTHOCORT Ophthalmic Ointment contains 1% CHLOROMYCETIN® (chloramphenicol, Parke-Davis), 0.5% hydrocortisone acetate, and 5,000 units polymyxin B sulfate per Gm., supplied in $\frac{1}{8}$-oz. tubes.

References: (1) Perkins, E. S. **Practitioner 178**:575, 1957. (2) Queries and Minor Notes. **J.A.M.A. 161**:1032, 1956. (3) Smith, C. H. **Eye, Ear, Nose & Throat Month. 34**:580, 1955. (4) Blakiston's New Gould Medical Dictionary, ed. 2, New York, McGraw-Hill Book Company, Inc., 1956, p. 945. (5) Ostler, H. B., & Braley, A. E. **J. Iowa M. Soc. 44**:427, 1954.



JUST RECEIVED!

newest model
of well known

HEINE GONIOSCOPE

In our opinion this is the finest Gonioscope on the market. It's easier to handle, has better, more brilliant illumination.

- **Prefocused, brilliant, air cooled light source.**
- **Precision German optics—6 times magnification.**
- **Rotating slit with easy fingertip control.**
- **Adjustable P. D.**
- **Modern design engineered for superb performance.**

AVAILABLE FOR IMMEDIATE DELIVERY!

Heine Gonioscope (as illustrated) Catalog No. X25-P1 ..... **$335.00***

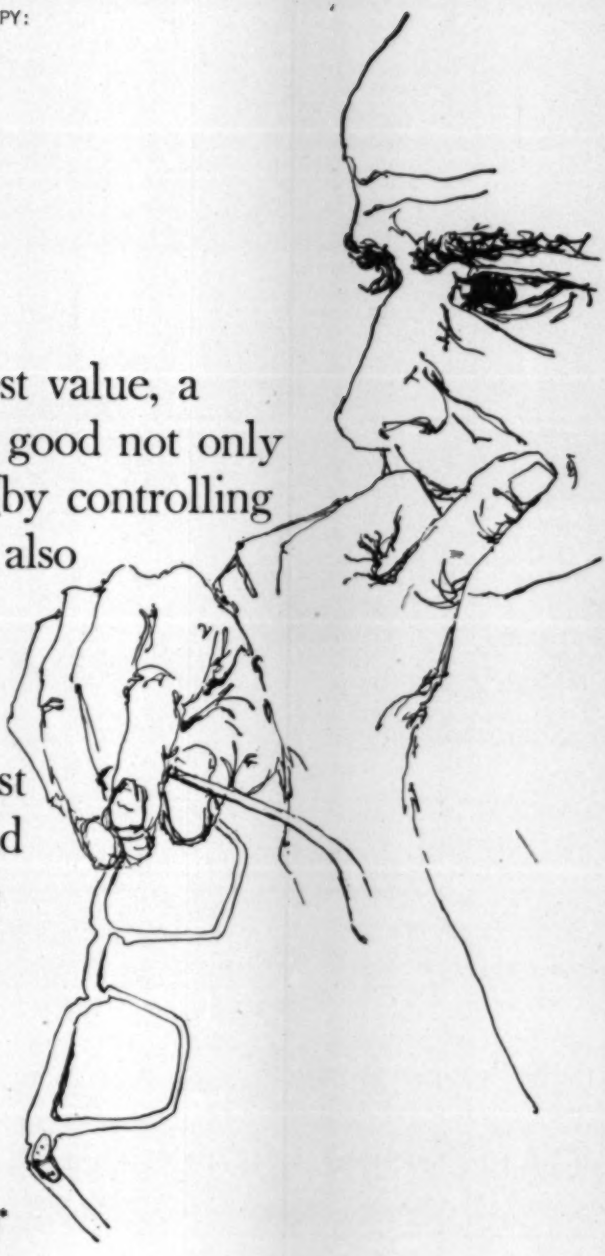
Heine Gonioscope complete with pulleys, counterweight and nylon cord, Catalog No. X25 ..... **$360.00***

***Prices include 5 amp. 6 volt transformer.**

The House of Vision Inc.

137 No. Wabash • Chicago 2, Illinois

REFLECTION ON CORTICOTHERAPY:



To be of greatest value, a steroid must be good not only for the patient (by controlling symptoms), but also to the patient (by minimizing side effects). To be of greatest value, the steroid should have the best ratio of desired effects to undesired effects:

Medrol*

the corticosteroid that hits the disease, but spares the patient

THE UPJOHN COMPANY
KALAMAZOO, MICHIGAN

Upjohn

*TRADEMARK, REG. U. S. PAT. OFF. — METHYLPREDNISOLONE, UPJOHN

at the pH of tears . . . No stinging or burning since Gantrisin Ophthalmic Solution is isotonic and is buffered at a physiological pH . . . stable and sterile. Antibacterially effective because Gantrisin Ophthalmic contains 4 per cent Gantrisin, the potent anti-infective . . . little likelihood of bacterial resistance. Multipurpose, because Gantrisin Ophthalmic is effective in common external ocular disorders, such as "pink eye" and nonspecific conjunctivitis, punctate and dendritic keratitis, superficial corneal ulcers, blepharitis . . . also consistently effective in many types of ocular trauma, for prophylaxis following surgery and after removal of foreign bodies.

GANTRISIN OPHTHALMIC SOLUTION

Available in 5-cc and ½-oz bottles with dropper.
Also available: Gantrisin Ophthalmic Ointment, in ⅛-oz tubes.

Gantrisin Diethanolamine Ophthalmic Solution and Ointment contain 4% Gantrisin®—brand of sulfisoxazole.
ROCHE®

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc • Nutley 10 • N. J.

Eyes Right!

the advantages of oil suspension

rapid even coverage on eye, lids, fornices . . . resists dilution by lacrimation . . . maintains effective antibiotic concentrations

the effectiveness of ACHROMYCIN

rapid suppression of common cocci and bacilli and of susceptible viruses—whether the primary infection or a complication of irritation, trauma, or inflammatory disease . . . fast resolution of swelling, erythema, and lesions . . . excellently tolerated

in the unique dropper-bottle

precise measurement of dose . . . clean . . . minimizes contamination . . . 4 cc. plastic squeeze dropper-bottle; 10 mg. (1%) ACHROMYCIN Tetracycline HCl per cc. sesame oil suspension

ACHROMYCIN®

Tetracycline Lederle

OPHTHALMIC OIL SUSPENSION 1%

Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, N. Y.

3 ophthalmic products with **distinctive advantages...**

- their wide-spectrum bactericidal activity includes *ALL clinically isolated strains of Pseudomonas aeruginosa,* a serious invader noted for the rapidity of its destructive powers.
- their component antibiotics rarely sensitize.

'NEOSPORIN'®

brand Polymyxin B-Gramicidin-Neomycin

ANTIBIOTIC OPHTHALMIC SOLUTION

Available in bottles of 10 cc. with sterile dropper.

'NEOSPORIN'®

brand Polymyxin B-Bacitracin-Neomycin

ANTIBIOTIC OINTMENT

Available in ⅛ oz. ophthalmic tubes.

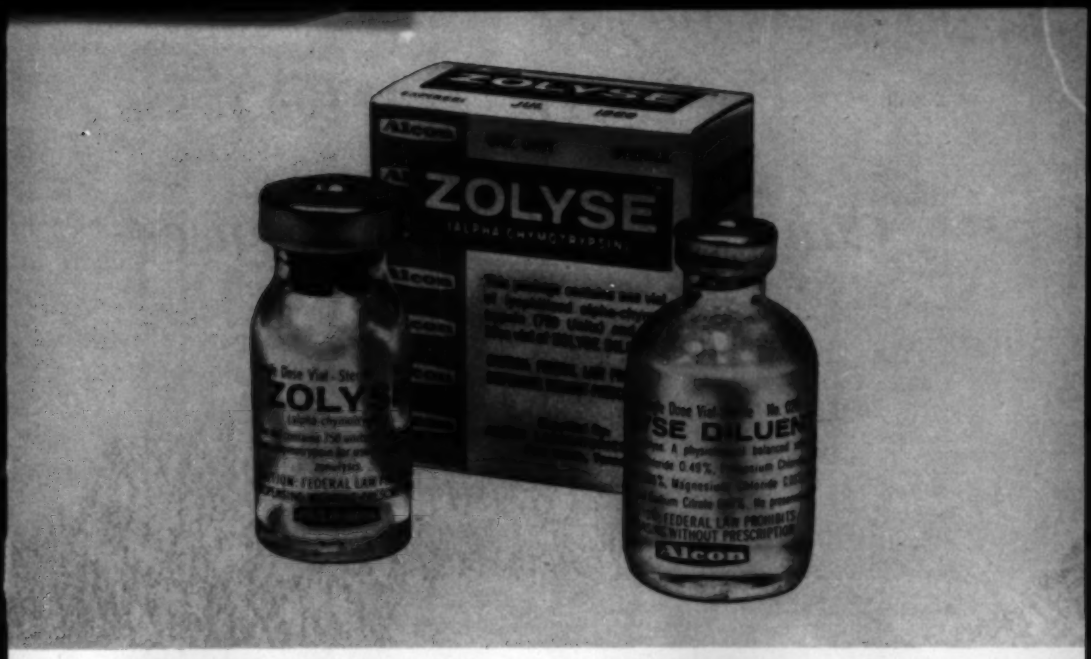
'CORTISPORIN'®

brand Polymyxin B-Bacitracin-Neomycin with 1% Hydrocortisone

ANTIBIOTIC OINTMENT

Available in ⅛ oz. ophthalmic tubes.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York



ZOLYSE™

alpha-chymotrypsin with BALANCED SALT SOLUTION, ALCON

In CATARACT SURGERY

ZOLYSE (alpha-chymotrypsin with BALANCED SALT SOLUTION, ALCON) selectively lyses the zonules, facilitates delivery of the lens and minimizes such dangers as capsular rupture, loss of vitreous, traumatic iridocyclitis and detachment of the retina.

The BALANCED SALT SOLUTION, ALCON, which is furnished as a diluent and for lavage purposes, is a sterile, physiological balanced salt solution containing those ions essential to normal cellular metabolism. This solution is more acceptable to the intraocular tissues[1] . . . and, in cataract surgery, seems to be more in balance with the normal fluids encountered in the inner eye.[2]

ZOLYSE is not recommended to be used under the age of 20 or in cases of fluid vitreous, subluxation of the lens, endothelial dystrophy or in traumatic cataracts where the hyaloid is not intact.[3]

Each ZOLYSE unit contains one vial of 750 units of lyophilized alpha-chymotrypsin and one 10cc vial of BALANCED SALT SOLUTION, ALCON, as the diluent and for irrigating the eye.

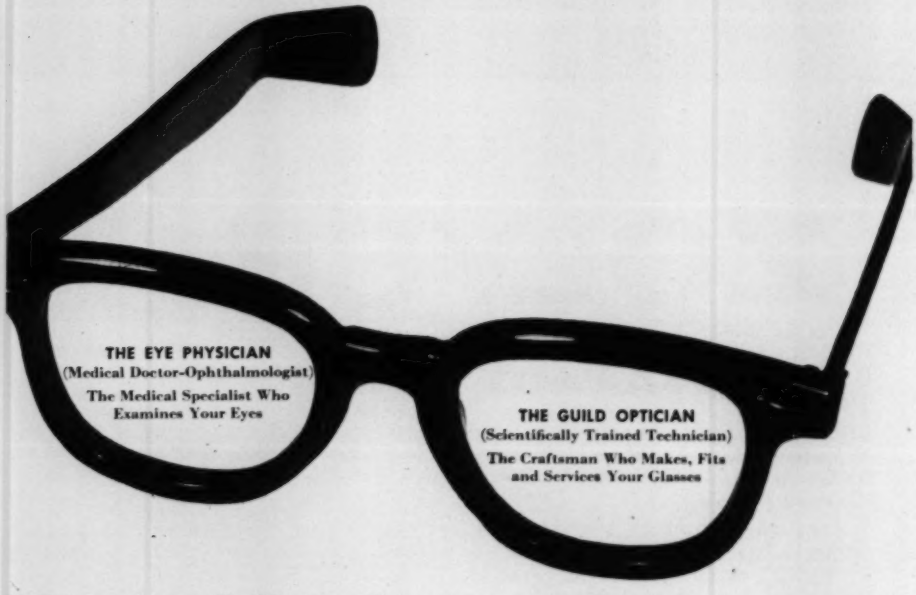
BALANCED SALT SOLUTION, ALCON, is now available separately in boxes of 36 for use in other ocular surgery.

[1] Girard, L. J., Dukes, C. D., and Fleming, T. C. Presented at the International Congress of Ophth., Brussels, Belgium, 1958.
[2] Kara, Gerald B., "The Use of Alpha-Chymotrypsin in Cataract Extraction," Research Report No. 10, Alcon Laboratories, Inc., 1959.
[3] Vail, D., et. al. Report: Committee on use of alpha-chymotrypsin in ophthalmology. Presented at the Sixty-fourth Annual Session, American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 11-16, 1959. (To be published)

Alcon ALCON LABORATORIES, Inc.
FORT WORTH, TEXAS

Can I Wear Contact Lenses Instead?

Let this Medical-Technical Team Help You Decide



FIRST, consult your Eye Physician (Ophthalmologist). He will give medical advice and analysis of your needs and if, after examination, he finds you can wear contact lenses he will prescribe the proper refraction and type of contact lenses best for you.

THE GUILD OPTICIAN will accurately fill the written prescription of your eye physician and work with you for as long as it takes to make you comfortable and confident in the handling care and wearing of contact lenses.

"renders extracapsular lens extraction unnecessary

Alpha
CHYMAR®
alpha chymotrypsin

a new approach to cataract surgery

Simple irrigation of the anterior and posterior chambers with Alpha Chymar loosens the zonule fibers within minutes without injury to any other structure of the eye. Removal of cataracts is thus greatly facilitated. In children, the risks of the needling operation are greatly reduced.

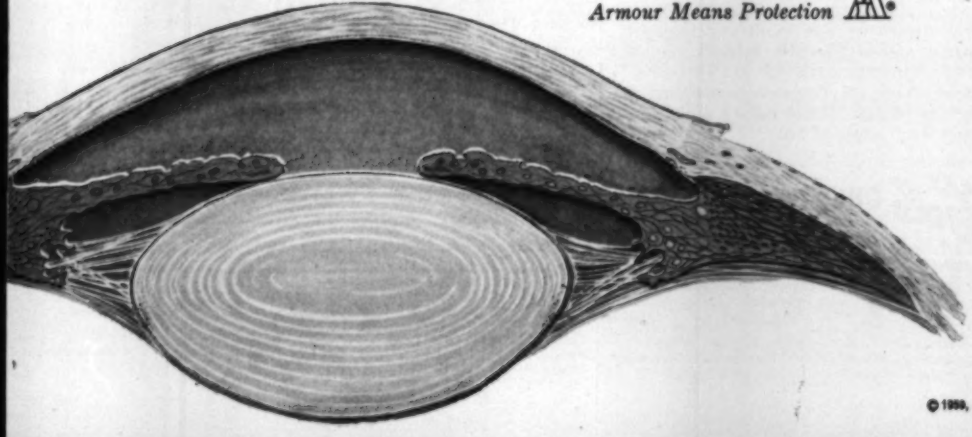
Alpha Chymar, a lyophilized crystallized chymotrypsin, has demonstrated its value as a new adjunct in cataract surgery in many hundreds of patients. [1, 2, 3, 4]

Specifically packaged for zonule lysis in lens extraction, ALPHA CHYMAR is available in cartons of 5 packages. Each package contains a 5 cc. vial of lyophilized ALPHA CHYMAR and a 10 cc. vial of ALPHA CHYMAR DILUENT (Sodium Chloride Injection, U.S.P.).

1. Cogan, J. E. H.: Proc. Roy. Soc. Med. 51:927, 1958. 2. Jenkins, B. H.: J.M.A. Georgia 45:431, 1956. 3. Raiford, M. B.: J.M.A. Georgia 48:163, 1959. 4. Rizzuti, A. B.: A.M.A. Arch. Ophth. 61:135, 1959.

ARMOUR PHARMACEUTICAL COMPANY • KANKAKEE, ILLINOIS

Armour Means Protection



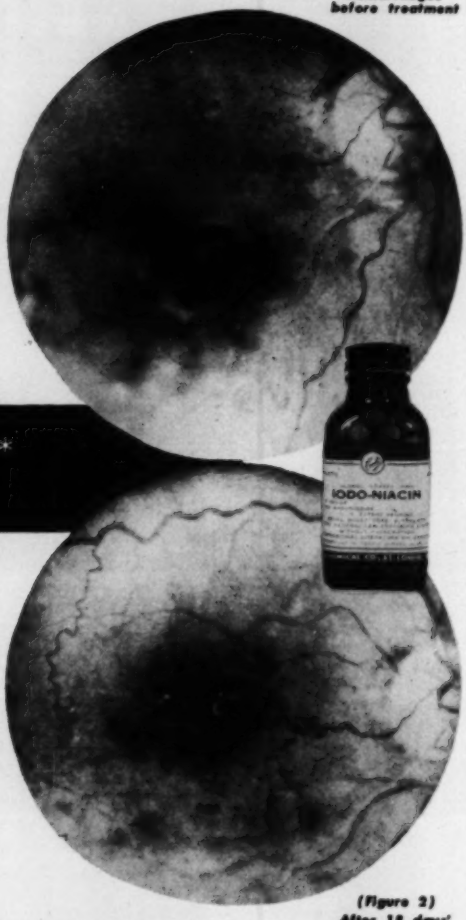
© 1959, A. P. Co.

retinal hemorrhages absorbed

with use of

IODO-NIACIN*

(Figure 1)
Retinal hemorrhages before treatment



(Figure 2)
After 18 days' treatment with Iodo-Niacin

NO IODISM

As shown by retinal photography, rapid absorption of retinal hemorrhages follows use of IODO-NIACIN. These results have been established in a series of 22 cases, 12 of retinal and 10 of vitreous hemorrhages.[1]

IODO-NIACIN Tablets contain potassium iodide 135 mg. (2¼ gr.) and niacinamide hydroiodide 25 mg. (⅜ gr.). The dosage used was 1 tablet three times a day. For greater effect this dosage may be doubled.

IODO-NIACIN may be administered in full dosage for a year or longer without any iodism or ill effect.[2]

In emergencies, for rapid and intensive action, IODO NIACIN Ampuls may be used intramuscularly or intravenously.[3] IODO-NIACIN Tablets are supplied in bottles of 100. Slosol coated pink. Ampuls 5 cc. boxes of 10.

Cole CHEMICAL COMPANY
3721-27 Laclede Ave., St. Louis 8, Mo.

1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.

*U.S. Patent Pending

Write for professional samples and literature

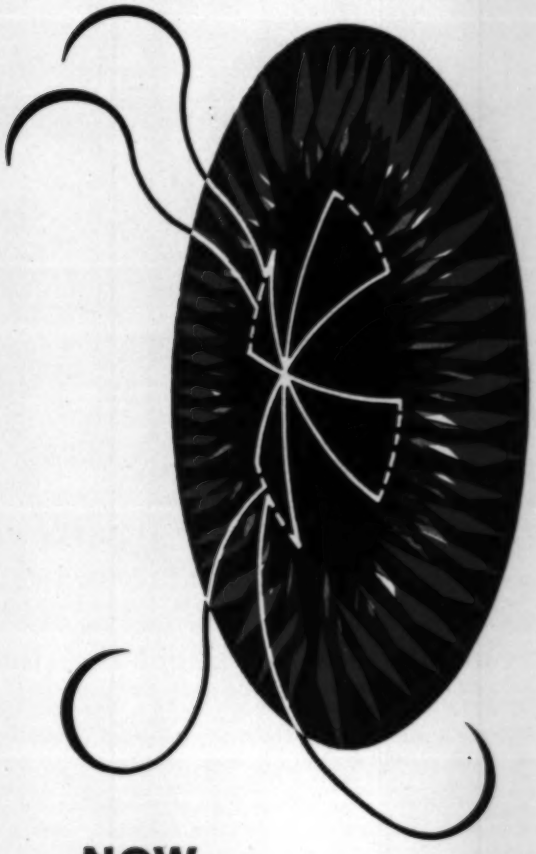
COLE CHEMICAL COMPANY AJO-1
3721-27 Laclede Ave
St. Louis 8, Mo

Gentlemen Please send me professional literature and samples of IODO NIACIN

_____ M.D.

_____ STREET

CITY_____ ZONE____ STATE_____



NOW...
UP TO 50% MORE STITCHES IN CORNEAL TRANSPLANT SURGERY

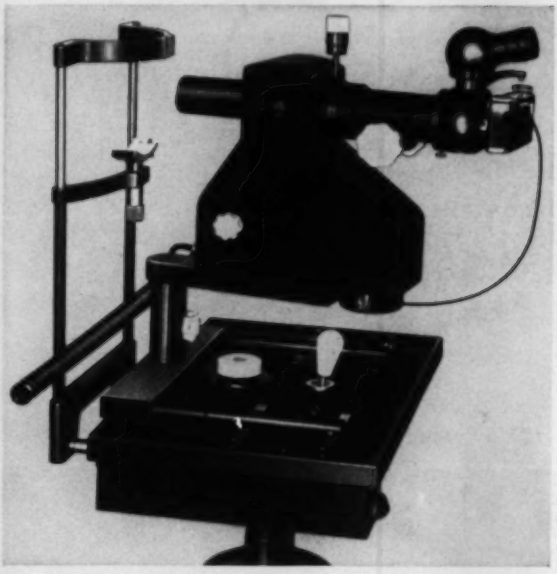
The new ETHICON G-5 NEEDLE, with its specially designed surfaces, eliminates cutting out in any direction. Its fine .008" gauge more closely approximates in size the 6-0 and 7-0 silk suture swaged to it, permitting more stitches, closer together, while reducing trauma. Flattened needle grasping area assures greater stability in the needle holder.

The 3/8 circle **G-5 NEEDLE** is another exclusive development in the ETHICON ophthalmic needle suture line designed specifically for ophthalmic requirements by ophthalmologists.

ETHICON®

CARL ZEISS
WEST GERMANY

FUNDUS CAMERA



Eye movement does not affect the picture

This camera photographs a circular fundus area with a diameter of 30°—in color or black-and-white. Movements of the eye do not affect picture definition because electronic flash permits a short exposure.

Diameter of the camera's illuminating pupil is adjusted to the diameter of the patient's pupil. Optically compensates for chromatic aberration and astigmatism of the eye.

Operation of the camera is largely automatic—shutter release switches from observation to photography. Can also be used as a measuring camera. Uses standard 35mm film.

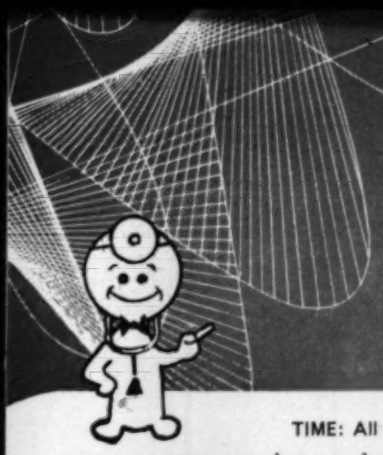
Other Carl Zeiss Equipment

Photo Attachments for Slit Lamp and Operation Microscope
Vertex Refractionometer • Diagnostic Set • Hand Lamp
Twin Lamp • Binocular Head Magnifier
Operation Microscope • Light Coagulator

Write for literature

CARL ZEISS, INC.
485 FIFTH AVENUE, NEW YORK 17, N. Y.

COMPLETE SERVICE FACILITIES



THE PLASTIC CONTACT LENS COMPANY

1960 COMPREHENSIVE CONTACT LENS SEMINARS

THREE-DAY SEMINARS / LENS ADJUSTMENT SEMINARS

TIME: All seminars will be held from 10 a.m. to 5 p.m. daily.

THREE-DAY SEMINAR: A comprehensive course of study designed to provide information and practical knowledge that can assist you in successfully fitting contact lenses. The latest techniques and developments will be presented such as fitting SPHERCON®, Bi-Curve and Tri-Curve lenses; the use of the new TORCON* lens in fitting unusual astigmia cases; the techniques of fitting BICON®, de Carle, and C. B. bifocal contact lenses; TELECON*, a recently introduced subnormal vision aid; Photo-Electronic-Keratoscopy (PEK*), its theory and use; CONTA-SONICS*, an invaluable aid to the practitioner.

To gain practical experience, each practitioner who registers for this course will receive a personal pair of contact lenses, which will be fitted in class. Your K-readings and Rx must be included with your registration so that your lenses can be processed prior to course date.

ONE-DAY LENS ADJUSTMENT SEMINAR: Provides the basic theory and practice required to perform all contact lens adjustments. This course to include: The CON-LISH* process of uniform edge finishing; methods of applying a CN bevel; grinding, polishing, and blending of intermediate and peripheral curves. The fundamentals of proper lens inspection will be fully demonstrated. Skill in lens inspection will enable you to objectively verify each lens adjustment you make.

SPRING 1960 SCHEDULE OF COMPREHENSIVE SEMINARS

Three-Day Seminars	Lens Adjustment Seminars	City and State	Hotel
February 23-24-25	February 26	Memphis, Tennessee	Peabody
March 1-2-3	March 4	Detroit, Michigan	Statler
March 8-9-10	March 11	Washington, D. C.	Statler
March 15-16-17	March 18	Salt Lake City, Utah	Utah
March 22-23-24	March 25	New York, New York	‡Vision Center
April 5-6-7	April 8	Los Angeles, California	Ambassador
April 12-13-14	April 15	Phoenix, Arizona	Westward Ho
April 19-20-21	April 22	Miami, Florida	McAllister
April 26-27-28	April 29	New Orleans, Louisiana	Jung
May 3-4-5	May 6	St. Louis, Missouri	Coronado
May 10-11-12	May 13	Dallas, Texas	Sheraton
May 24-25-26	May 27	Boston, Massachusetts	Sheraton-Plaza
June 7-8-9	June 10	Montreal, Quebec	Queen Elizabeth
June 14-15-16	June 17	Philadelphia, Pennsylvania	Sheraton
June 21-22-23	June 24	Denver, Colorado	Brown Palace

*Trademark

‡This Seminar will be held at the Wesley/Jessen Contact Lens Company, Vision Building, 635 Madison Ave., New York 22, N.Y.

SEMINAR REGISTRATION FORM

Please mail to THE PLASTIC CONTACT LENS COMPANY, 5 South Wabash Avenue, Chicago 3, Illinois. A $25.00 DEPOSIT IS REQUIRED WITH ALL REGISTRATIONS. CHECK THE SEMINAR YOU DESIRE TO ATTEND:

Note: If registering for the Three-Day Course, be sure to include your K-readings and Rx so we may process your lenses prior to seminar date.

DUCTUS DEDICATIONE / LEADERSHIP THROUGH DEDICATION

☐ Enclosed is my registration check for $65.00 for the Three-Day Contact Lens Seminar.

☐ Enclosed is my registration check for $27.50 for the One-Day Lens Adjustment Seminar.

(Date of Seminar) _____ City _____

Name _____

Your Mailing Address _____

City _____ Zone _____ State _____

RECORD K-READINGS AND YOUR RX HERE:

K-Readings: O. D. _____ O. S. _____

Refraction: O. D. _____ O. S. _____

THE PLASTIC CONTACT LENS COMPANY
5 South Wabash Avenue, Chicago 3, Illinois

with ORTHOGON lenses...the extra

YOUR PATIENT has every right to all the pleasure he or she can get from a new pair of glasses . . . good appearance, comfort, and most of all, the best possible in vision.

Because of their fundamental design, their correction system, and the superb quality of their manufacture, the single-vision series of Orthogon corrected-curve lenses provides the best in vision that science can offer.

For you to furnish tangible evidence of such quality is to indicate your concern for your patient's visual welfare.

"For Vision at its Best" tells your patient

TAKE CARE OF THEM . . . Like eyes themselves, your glasses are a precision instrument. Treat them accordingly. Never rest them with the lenses face down; with care you can preserve the high lustre they have now. Keep them in a case when not in use.

atisfaction of knowing

ll he needs to know . . . and no more . . . bout the care with which his prescription vas prepared.

It becomes a quiet, dignified means of elling your patient that you demand the very best in materials. It is more than a ourtesy . . . it is the essence of good profes-ional relations.

The folder covers three points: (1) the care of glasses, (2) a mention of diversified vision needs, and (3) a certification of lens and prescription quality.

If you are not now familiar with it, ask your supplier to show you a sample copy of "For Vision at its Best." It is available automatically with every Orthogon prescription from your regular supplier of B&L ophthalmic materials.

BAUSCH & LOMB

SINCE B&L 1853

EP THEM CLEAN . . . Wash your glasses every day with soap and warm water. A all, soft brush may be used to clean the hard-to-reach parts. Dry with a soft cloth or ue. Have your glasses adjusted periodically, and never attempt repairs on your own.

CHECK CONTACT LENS RADIUS
in just 4 EASY STEPS
with New AO Radiuscope

Now its possible to measure the radii of curvature of contact lenses...both concave and convex surfaces. You can even measure lens thickness with the AO Radiuscope. The fine quality optical system and extra sensitive micrometer mechanism gives you extremely accurate measurements...so desirable in preparing to fit contact lenses. You can be sure that your prescription has been followed precisely. The few moments it takes to check, can save possible re-calls and re-fitting later. Here's all you do to measure a concave curve.

1 Turn adjustment knob *down* to focus on top surface of lens positioned in mount. At the same time a built-in target will be visible. Bring this target into sharp focus.

2 The dial gage zeroing knob is turned until a zero reading appears on the small inner dial and the large outer dial.

3 Focusing adjustment knob is turned *up* (counter-clockwise) until a second target image appears. Bring this image into sharp focus.

4 Take measurement reading. First read small inner dial...then large outer dial. Adding both figures will give you the curvature of lens surface in hundredths of millimeters.

American Optical
COMPANY
INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. A253
Yes, I would like to see how the New AO Radiuscope can make my contact lens measuring job easier.
☐ Please send full information by return mail.
☐ Have my AO Sales Representative or Supplier call.

Name _____
Address _____
City _____ Zone _____ State _____

Use the AO Ophthalmometer for easy, accurate measurement of corneal radius

Here's why the AO Micromatic Ophthalmometer is the ideal instrument for determining corneal radius in your contact lens work. It is quick, easy and absolute. With a single setting of the power wheel you can find the radius of curvature as well as the dioptric power of the principal meridian under test.

You can do this *only* with the AO Ophthalmometer because only this instrument has the radius of curvature scale engraved in millimeters on the side of the power wheel. You take both readings . . . radius in millimeters or power in diopters . . . directly from the scale. Bothersome conversion tables are unnecessary.

It's unexcelled for routine refraction procedure, too. In the case of astigmatic cornea, the AO Ophthalmometer locates the axis and computes the difference in power between the meridians of greatest and least power. This is essential in cases where irregular retinoscope shadows introduce uncertainities . . . where low acuity reduces the adequacy of subjective judgements . . . and where high errors make precise determination of axis imperative.

Contact your AO Representative or Supplier to arrange a demonstration at your convenience . . . or send handy coupon for further information.

American Optical
COMPANY
INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. A253
Please send full information on AO Ophthalmometer.

Name_____

Address_____

City_____ Zone____ State_____

AROUND THE CLOCK CONTROL IN GLAUCOMA?

Do present short acting miotics control chronic simple glaucoma "around the clock"? Is the intraocular pressure normal during the day but elevated every night when treatment is interrupted? Is a gradual loss of visual fields the inevitable consequence of a failure to maintain control 24 hours a day? . . .

While these questions are being investigated by a number of research groups and the final answers are not yet available, it appears that long acting Phospholine Iodide is a significant advance toward the ideal of "around the clock" control.

Other advantages of Phospholine Iodide are: improved control of difficult cases, user convenience leading to better patient cooperation, economical packaging for hospital or clinic.

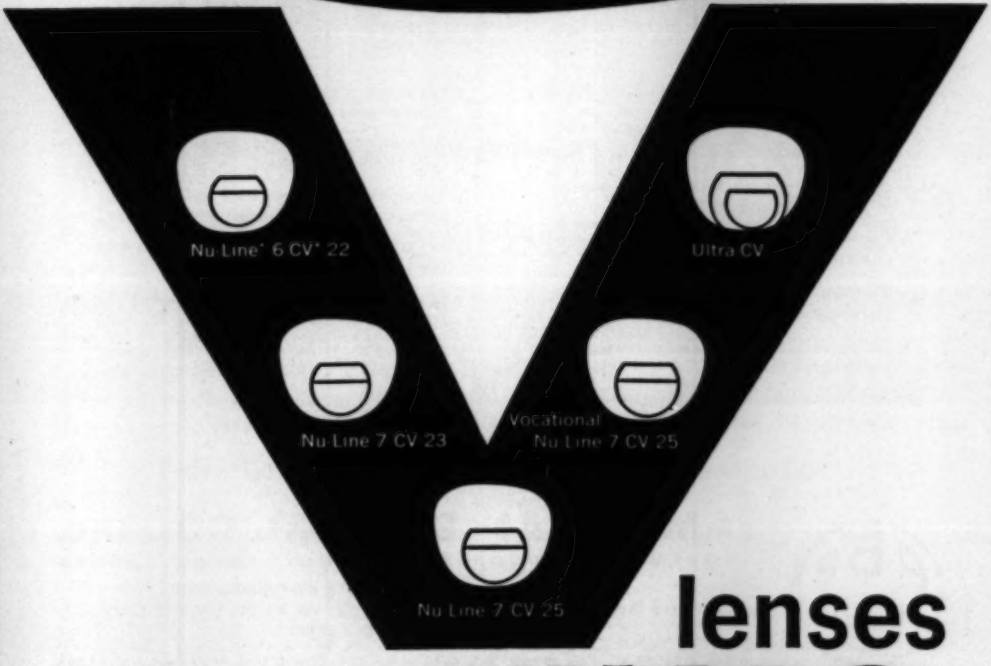
Aqueous solutions are freshly prepared for each prescription and are stable for one month at normal room temperature or 6 months in the refrigerator. Unopened package never requires refrigeration.

Phospholine Iodide

CAMPBELL PHARMACEUTICALS, INC., 121 East 24th St., New York 10, N.Y.

for most presbyopes

the only way
to get Excellity* performance
in the area 18" to 50"
from the eyes—
UNIVIS Nu-Line Continuous Vision*
lenses



lenses
UNIVIS

IDENTIFIED — Look for the faint brownish-pink coloration* of the segment line

*Trademarks of The Univis Lens Company • Dayton, Ohio

a new cataract lens that lets aphakic patients *SEE* the difference!

FIRST ASPHERIC

GLASS

CATARACT LENSES

VOLK

Catra *Conoid*

BIFOCALS

AMERICAN BIFOCAL CO., INC.

Now Patients Can Have Clear Vision from Edge to Edge . . . . Check These Advantages

√ Crown glass enables precision grinding and permanent surface curvatures required for ideal correction of lens aberration.

√ Abrasion-resistance of crown glass insures long, useful life.

√ Crown glass and aspheric curves reduce chromatic aberration.

√ Elimination of distortion of both stationary and moving objects.

√ Uniform magnification increases peripheral vision.

√ All aberrations optimally corrected for every lens power.

√ Aspheric curves permit lens to be thinner and lighter.

√ Patient's eye appears normal and undistorted to others.

√ Elimination of marginal astigmatism gives clear, wide-field reading vision.

√ A large 22mm straight-top, color-free reading segment is incorporated.

√ Lenses are available in semi-finished form for completion by local Rx lab.

√ Local laboratory may resurface inner spherical side of lens when necessary.

√ Patient's post-operative adaptation to cataract lenses is easier.

VOLK CATRACONOID LENSES ARE AVAILABLE IN 50mm DIAMETER

AMERICAN BIFOCAL CO., INC.

FOREMOST PRODUCERS OF MULTI-FOCAL LENSES

Exclusive Manufacturers of:

VOLK CONOID LENSES FOR SUBNORMAL VISION
VOLK CONOID LENSES FOR INDIRECT OPHTHALMOSCOPY
VOLK CATRACONOID BIFOCALS

1440 ST. CLAIR AVENUE, CLEVELAND 14, OHIO

NEW MODEL

Harrington-Flocks Field Screener only $149.50

Introduced by Jenkel-Davidson in 1956, the Harrington-Flocks Visual Field Screener has become standard equipment in leading ophthalmologists' offices throughout the country.

This Screener has proved to be remarkably accurate—and you can easily test a patient in three to five minutes! No special instructions are needed. Just press a button activating the black light flashes. What the patient sees on the various test cards indicates any loss in visual field, signaling the necessity of further tests for glaucoma and other diseases.

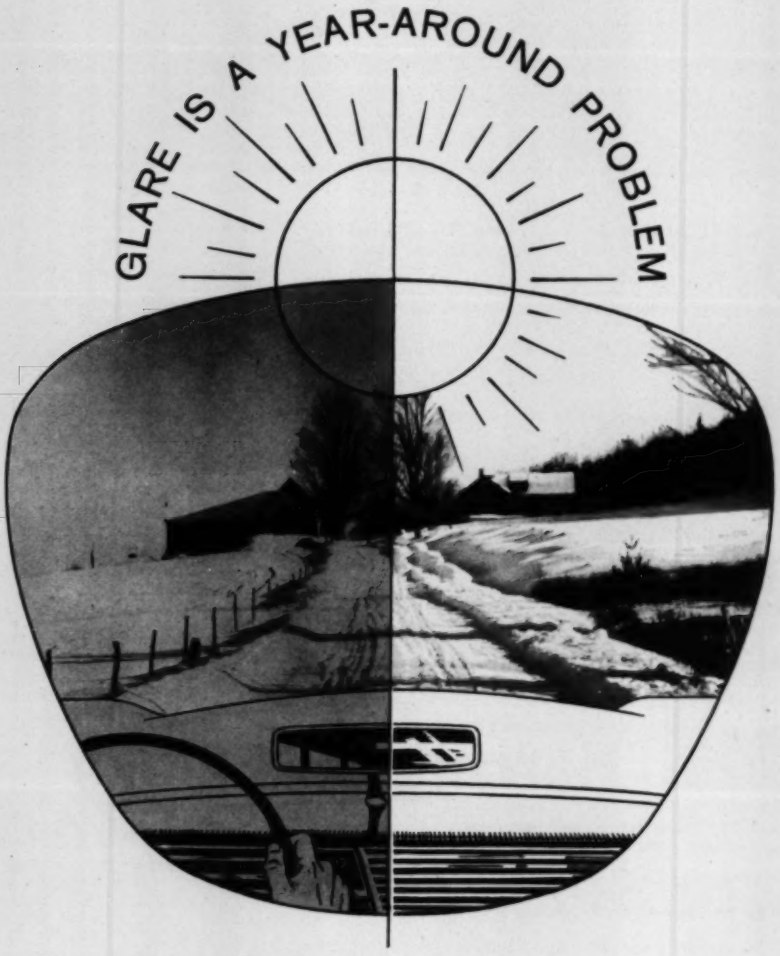
Order today—take advantage of this new low price.

Satisfaction guaranteed. Write or wire collect

Jenkel-Davidson
OPTICAL COMPANY

366 Post Street • San Francisco, California

5824



People Need

WINTER*EYES*ING TOO!

Give your patients scientific glare protection year around with Titmus Sun Wear . . . THE ONLY COMPLETE SUN WEAR LINE SOLD EXCLUSIVELY TO YOU—THE PROFESSION!

TITMUS OPTICAL COMPANY, INC., PETERSBURG, VIRGINIA

CARL ZEISS

. . . THE ONLY TOPAZ TINTED LENSES THAT GIVE GLARE AND SUN PROTECTION

Zeiss UROPAL lenses, with fully corrected curve, are renowned throughout the world for their quality and they are the only lenses, with light tint, that filter out the harmful ultra violet and infra-red rays. The topaz tint is cosmetically becoming to the wearer and gives the impression of lightness and brilliance which is so helpful to the sight even in artificial light without the penalties imposed by invisible rays, which come from all sources of light.

There is nothing like Zeiss Uropal for everyday wear.

ZEISS PUNKTAL LENSES . . . classic white lenses that give a point focal image and broad field of vision throughout the lenses, are available in a wide range of powers.

ZEISS UMBRAL LENSES . . . give perfect eye protection, in summer and winter, against excessive glare and infra red and ultra violet rays, yet the even brown tint retains colors in their natural proportions.

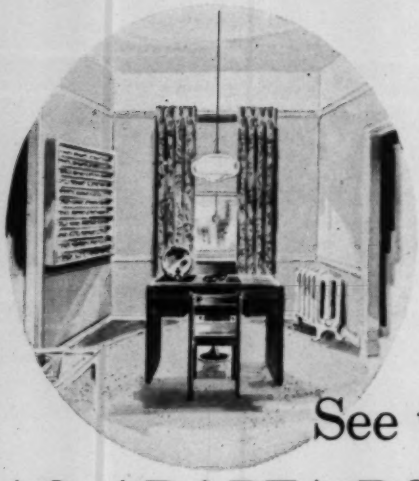
TO BE SURE . . . dispense the finest . . . specify ZEISS LENSES for all your patients.

For your protection every lens bears this symbol of perfection.

Sole agent in the U.S.A.

TRANS-CONTINENTAL OPTICAL CORP.

2315 BROADWAY, NEW YORK 24, N.Y.



See what a difference AO ADAPTA-ROD FURNITURE can make in an office!

More storage room . . . added convenience . . . a partition for privacy . . . beautiful new "custom-look" furniture!

Does your professional office need modernizing? . . . separate fitting rooms? . . . additional frame bars? . . . extra working space for personnel? . . . attractive storage space for frames, instruments, catalogs, reference materials?

You can solve these problems easily with American Optical's beautiful new ADAPTA-ROD cabinets and sturdy ADAPTA-ROD structural supports. And if you like, you can use the cabinets as separate units with 6" legs. It's the new, modern way to give your office that attractive, custom-designed look . . . *economically.*

ADAPTA-ROD cabinets in Novoply birch have the warm wood tones and clean styling that blend perfectly with either traditional or contemporary decor. They are sturdily constructed, have almost indestructible Formica tops, and their tough, durable finishes remain lastingly beautiful. Spacemakers include:

Roomy Sliding Door Cabinets—24" and 14" heights. Just right for larger boxes and instruments.

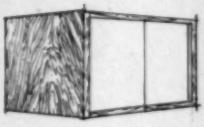
Matching 5-Drawer Cabinet—Plenty of space for frames, lenses and small items.

Convenient Frame Bar—30"x48". Three rotating panels put up to 90 frames at your fingertips.

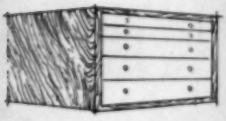
ADAPTA-ROD cabinets are the practical answer to space problems in your office. They're easy to have, too, with the American Optical Pay-As-You-Grow Plan. Take up to five years to pay for the office you want now. Mail coupon today for details.

American Optical
COMPANY
Since 1833 . . . Better Vision for Better Living

Frame Bar with
Rotating Panels



24" Sliding Door Cabinet



5-Drawer Cabinet

14" Sliding Door Cabinet

American Optical Company
Dept. 4631, Southbridge, Mass.

Please send me a copy of your brochure, *"AO Adapta-Rod Furniture for Professional Offices."*

NAME_____

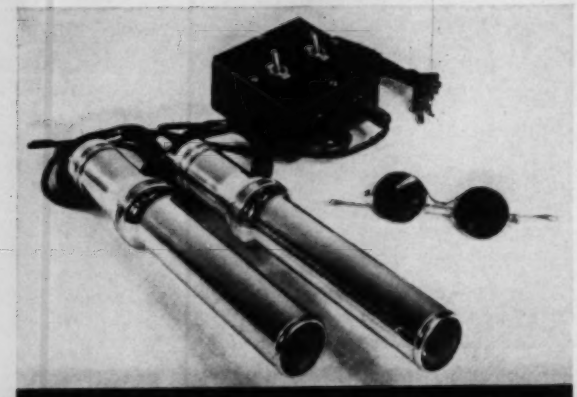
ADDRESS_____

CITY_____ ZONE____ STATE_____

THE Allied

STRABISMOMETER

and Basic Fusion Trainer

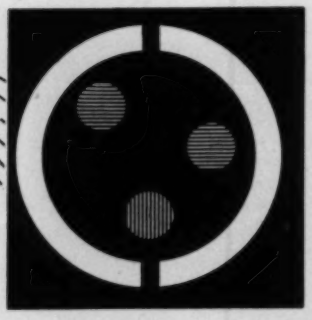


Quick-Easy Diagnosis

- **Quick, accurate measure of subjective angle of deviation**
- **Effective diagnosis of paresis of ocular muscles**
- **Effective with children as young as 3 years of age!**

Write for reprint of article on "Isolated Cyclovertical Muscle Palsy"

THE NEW RING FUSION TEST



Rapid efficient post-surgical test of peripheral fusion at all distances . . .

See this STRABISMOMETER and also the RING FUSION TEST by Allied in our INSTRUMENT DEPARTMENT.

The House of Vision Inc. 137 NORTH WABASH CHICAGO 2, ILLINOIS

AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3 · VOLUME 49 · NUMBER 1 · JANUARY, 1960

CONTENTS

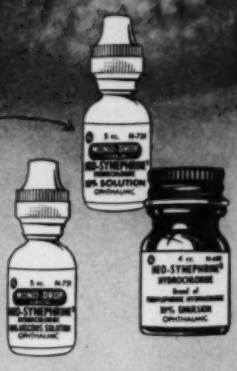
when the eyes have it

There are five dosage forms of Neo-Synephrine hydrochloride especially formulated for vasoconstriction and mydriasis in ophthalmologic conditions.

½% solution

Decongestant collyrium for rapid relief of burning, itching and smarting.

Available in convenient Mŏno-Drop squeeze bottles that eliminate dropper contamination and simplify instillation.*



2.5% solution for short acting mydriasis in refraction, ophthalmoscopy, surgery and the treatment of glaucoma.

10% solution (plain or viscous) and emulsion

In uveitis: With atropine, for freeing recently formed posterior synechiae and preventing their formation.
In glaucoma: For temporarily reducing intra-ocular tension and for performing the provocative test for angle block.
For use in surgery.

NEO-SYNEPHRINE®
Hydrochloride

wide application in ophthalmology

Winthrop LABORATORIES • NEW YORK 18, N. Y.

*Mono-Drop, trademark

Neo-Synephrine (brand of phenylephrine), trademark reg. U. S. Pat. Off.

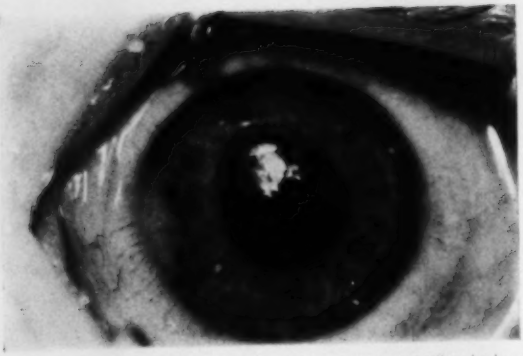


Fig. 1 Case 1 (L. A.) Nevoxantho-endothelioma of iris and ciliary body. December 3, 1953.

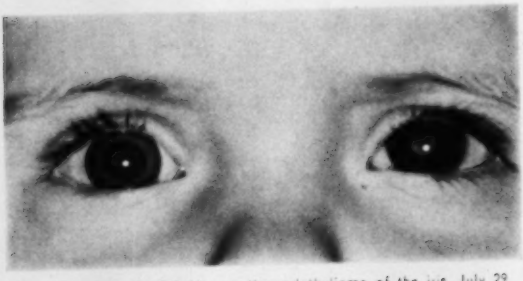


Fig. 3. Case 2 (E. O.) Nevoxantho-endothelioma of the iris. July 29, 1957.

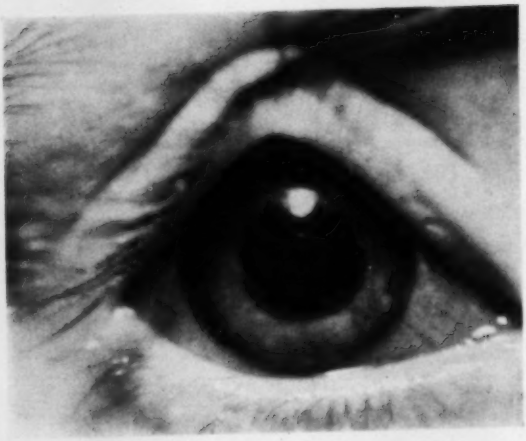


Fig. 6. Case 2. (E.O.) April 19, 1958. Note slate-gray appearance of left iris after lesion has subsided.

Figs. 1, 3 and 6 (Maumenee and Longfellow). Treatment of intraocular nevoxantho-endothelioma.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 49 JANUARY, 1960 NUMBER 1

TREATMENT OF INTRAOCULAR NEVOXANTHO-ENDOTHELIOMA*

(JUVENILE XANTHOGRANULOMA)

A. EDWARD MAUMENEE, M.D.
Baltimore, Maryland
AND
DONALD W. LONGFELLOW, M.D.
Washington, D.C.

Five cases of ocular lesions associated with nevoxantho-endothelioma have been reported.[1-4] In four of these, the anterior uveal tract has been affected and in one the epibulbar tissue. The uveal involvement produces a brownish to yellow thickening of the iris, secondary glaucoma, and usually anterior chamber hemorrhage. The one case of epibulbar lesion began as small yellowish masses at the limbus similar to phlyctenules. Over a period of four months the lesion in both eyes enlarged to produce a four mm. diameter elevated yellowish mass which extended over the surface of the cornea.

All the uveal lesions were initially observed during the first five months of life. The epibulbar lesion was first observed at the age of three and a half years. In three instances the eyes with uveal tract involvement were enucleated because of suspected tumor and secondary glaucoma. In one patient the globe was apparently saved by a trephining operation for glaucoma but there was no mention of the condition of the eye nor the duration of observation after the operation.[3]

The two cases to be reported at this time are of interest because to our knowledge they are the first in which the iris lesion has subsided under treatment.

CASE REPORTS

CASE 1

L. A. (S. U. H. 331456). The patient was a three-year-old white girl whose first ocular symptoms began in August, 1953, when she had a small fleck of blood near the pupillary border at the 12-o'clock position on the iris of the left eye. This cleared in about two weeks and she had no further difficulty until the first of October when her left eye again became irritated. She was seen by Dr. Frederick W. Kraft* on November 21st, and it was noted that she had heterochromia of her left iris. There was also a small yellowish-brown, lipoidal appearing tumor at the 9-o'clock position near the root of the iris.

The patient was first seen in consultation on November 27, 1953, at the Stanford University Hospital. Examination at that time revealed the right eye to be entirely normal. The left eye was photophobic and showed a mild circumcorneal congestion and a slight flare of the aqueous. The iris in the right eye was light blue to hazel in color, the iris in the left eye was dark and appeared to have a more brownish color. At the root of the iris on the nasal side from about the 10:30- to 8-o'clock position there was a yellowish-brown elevated mass which extended forward from the surface of the iris to touch the posterior surface of the cornea. Elsewhere in the iris there were several yellowish brown plaques of thickened iris stroma (fig. 1). Newly formed or dilated blood vessels could be seen on the iris in these areas. The aqueous ray was positive and there were a few fine keratic deposits on the posterior surface of the cornea.

Examination under ether anesthesia revealed the

* From The Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University, and the Walter Reed Army Hospital. The page of colored reproductions is sponsored by the Alcon Laboratories, Inc., Fort Worth, Texas. This is the first of two such pages, which will appear in THE JOURNAL to determine if contributors would like to have such a page made available to them each month without charge to the author.

* This case is reported by the kind permission of Dr. Frederick W. Kraft of Salinas, California.

tension to be normal in both eyes. On ophthalmoscopic examination with scleral indentation it was found that the iris tumor, on the nasal side, extended through the thickness of the iris, impinged on the anterior surface of the lens, and extended back into the ciliary body.

Because of the unusual appearance a malignant tumor of the iris was suspected. Therefore, an attempted biopsy of the nodule on the nasal side was undertaken. A small conjunctival flap was raised and a four-mm incision was made into the anterior chamber angle. Repeated attempts to biopsy the tumor revealed it to be extremely friable and only a few one-mm. pieces of tissue could be obtained. Further efforts to excise the tumor were not attempted because of the fear of producing a massive anterior chamber hemorrhage.

Histologic examination of smears taken from the anterior chamber and of the small bits of tissue removed revealed a variety of cells consisting of neutrophils, leukocytes and monocytes. The principal cell in the lesion, however, was the histiocyte (fig. 2).

The patient was given topical cortisone drops to the left eye and discharged from the hospital. She was not seen again until January 25, 1954, when it appeared that the iris was more extensively involved with many yellowish-brown nodular areas of infiltration. It was suspected that the patient had a lymphoma of the iris.

General physical examination revealed multiple yellowish papillomacular lesions over the abdomen and back. The remainder of the examination except for her eyes was essentially normal.

Skin test with 1/1000 old tuberculin was negative. Bone-marrow examination was normal. Hemocytology revealed 5.1 mil RBC, hemoglobin of 13.2 gm. per 100 cc.; a white blood count of 7,150 and a differential count of 35 percent neutrophils, 53 percent lymphocytes, nine percent monocytes and three percent eosinophils. The platelet count was 288,000.

On January 27th, the child was again placed under general anesthesia. A tap of the anterior chamber was done and the aqueous centrifuged for cells. Again lymphocytic cells, wandering cells, and eosinophils were noted.

The patient was given 600 r of X rays with the following physical factors: KVP 50, MA 20, TSD 1.8 cm. and no filtration. The HVL was 0.28 mm. of Al. The treatment fields were confined to the iris and nasal side of the globe.

The patient was discharged from the hospital and was continued on topical hydrocortisone therapy. She was seen again on March 16, 1954, at which time the iris lesion was still present, but appeared less prominent than on previous examinations. On January 15, 1955, Dr. Kraft reported that the lesion had not changed appreciably. By March 1st the lesion had practically disappeared from the iris; and, on April 12th, the thickness of the iris was normal. The circumcorneal injection had disappeared and the child was no longer photophobic.

On June 20, 1958, the sclera and conjunctiva were normal. There was no suggestion of a retro-iris mass. In the area of the biopsy the iris was slightly atrophic and was a little grayer in color than the remainder of the iris. Pupillary reaction was normal. There were a few anterior subcortical opacities in the periphery of the lens. The fundus

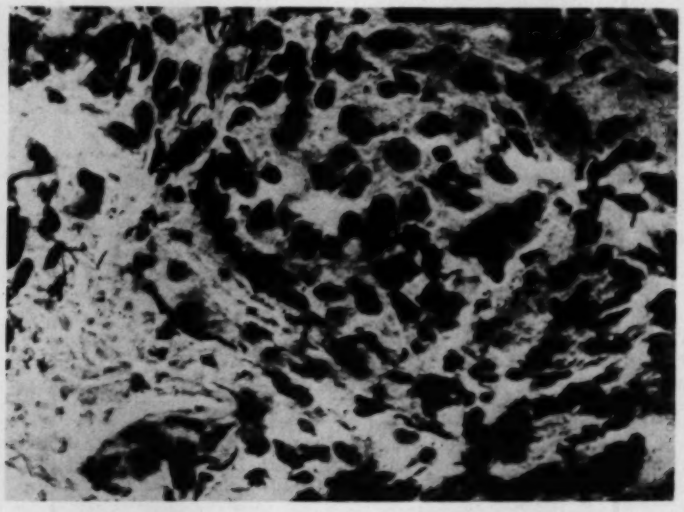


Fig. 2 (Maumenee and Longfellow). Case 1. Biopsy of iris, showing histiocytic infiltration. (×650.)

was easily seen and appeared normal. Visual acuity in the right eye was 20/50 with a lens of +4.25D. sph. ⌒ −2.75D. cyl. ax 13°, and in the left eye 20/20 with a lens of +1.0D. sph. ⌒ −0.5D. cyl. ax. 180°.

The diagnosis of nevoxantho-endothelioma in this child was not suspected until April, 1956. A review of the clinical notes taken in 1953 and of the small piece of iris obtained at biopsy suggested this as the most probable diagnosis.

CASE 2

E. M. Q. (W. R. A. H. 5477037). The patient was an 11-month-old white girl who was first admitted to the Walter Reed Army Hospital on July 13, 1957. A history was obtained that her eyes were entirely normal until May 6, 1957, at which time a small hyphema was noted in the left eye. The hemorrhage cleared in six days but, on May 23rd, a second anterior chamber hemorrhage appeared. Routine laboratory work including X-ray films, fasting blood sugar, and a complete blood count were all within normal limits. After she was discharged on May 25th, the hemorrhage gradually absorbed. On June 14, 1957, a third hemorrhage appeared in the anterior chamber accompanied by a moderate circumcorneal congestion and photophobia.

On July 13, 1957, she was admitted to the Walter Reed Army Hospital. General physical examination revealed the child to be entirely normal except for her skin and ocular lesions. There was no evidence of enlargement of the liver or spleen. Neurologic examination was within normal limits. Examination of the skin revealed several orange yellowish macular lesions which appeared to be lipomas. Dermatologic consultation confirmed these lesions as xanthomas and a diagnosis of nevoxantho-endothelioma was made.

Ocular examination revealed the right eye to be entirely within normal limits. The iris of the left eye had a muddy appearance with dilated vessels in the 11- and 3-o'clock positions (fig. 3). The tension was not elevated nor was the cornea steamy. A diagnosis of nevoxantho-endothelioma of the iris or heterochromic iridocyclitis was made.

Hematologic examination revealed a white count of 12,500, differential of 36 percent neutrophils, 65 percent lymphocytes and two percent eosinophils. Hemoglobin was 12.2 and hematocrit 34.5. Urinalysis was entirely negative. On August 12, 1957, the serum cholesterol level was 212 mg. percent.

On July 29th, one of the skin lesions which had previously been biopsied was biopsied a second time (figs. 4 and 5). A frozen section of the material was stained for fat and embedded in gelatin. Histologic examination of this and other material revealed a central scar, presumably the site of the previous biopsy. At the periphery of the scar the corium was infiltrated by spindle and polygonal-shaped cells which contained material that stained positive with a fat stain. There was also a slight admixture of chronic inflammatory cells. Touton giant cells were not present and eosinophils were inconspicuous. The xanthogranulomatous infiltrate caused a thinning of the overlying epidermis.

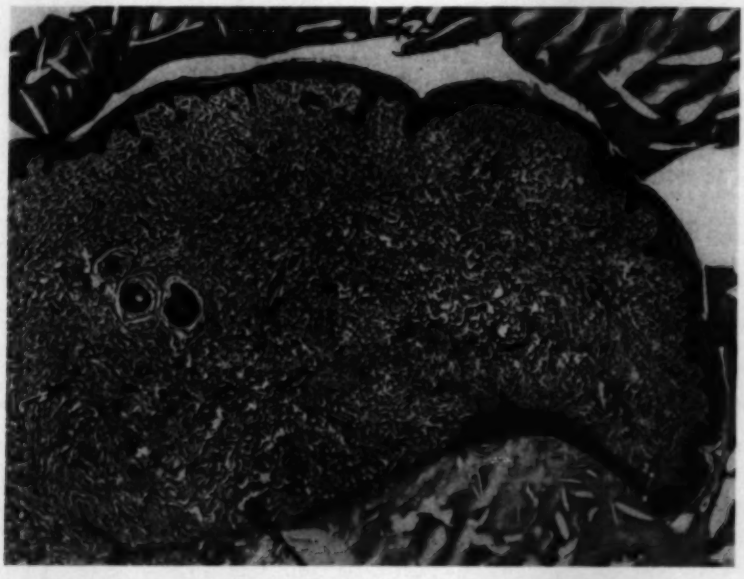


Fig. 4 (Maumenee and Longfellow). Case 2. Biopsy of skin lesion. (×56.)

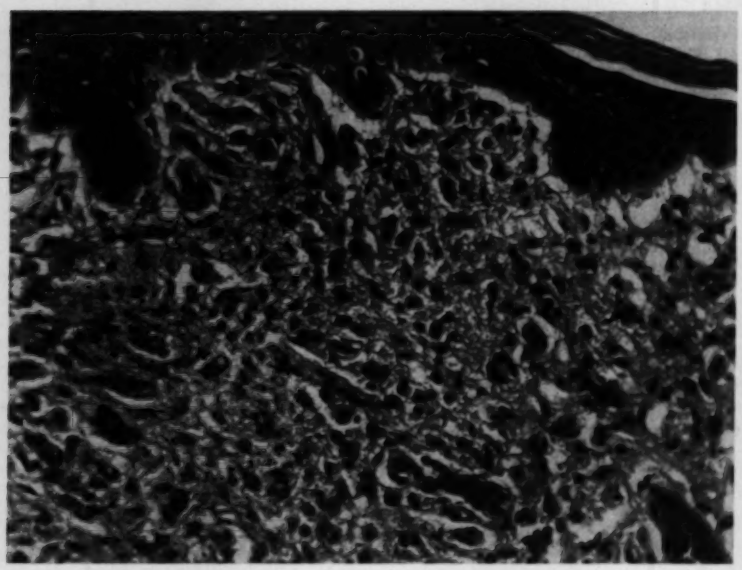


Fig. 5 (Maumenee and Longfellow). Case 2. Biopsy of skin lesion, showing histiocytic infiltration of corium. (×330.)

Dr. Elson B. Helwig interpreted this material as follows:

"It is probable that this lesion represents a nevoxantho-endothelioma or juvenile xanthogranuloma. According to the information available, the present biopsy represents material excised from an area that was previously biopsied. The reaction in general is consistent with that noted in juvenile xanthogranuloma and the inflammation within the adjacent corium probably can be accounted for on the basis of the previous biopsy."

On July 31, 1957, it was noted that the ocular pressure in the left eye was elevated. The patient was placed on pilocarpine and Diamox. Repeated tensions under seconal sedation ranged from 80 mm. Hg to 35 mm. Hg (Schiøtz). On August 9th, a goniopuncture was performed on the left eye. This operative procedure reduced the ocular tension but it still ranged between 20 and 30 mm. Hg (Schiøtz). On August 14th, the patient was placed on systemic cortisone therapy in addition to pilocarpine and Diamox. From August 25th through August 30th five treatments of 100 r were given to the left eye for a total dose of 500 r. The factors in the X rays were 200 KV, 20 MA, HVL 1.0 mm. Cu, TSD 50 cm. The radiation was delivered through five-cm. circular fields.

On October 9th, the cornea was slightly hazy, the iris still had a brownish-yellow, muddy, thickened appearance. At the 3 o'clock position in the corneal periphery there was a scar from the previous puncture, and in the area of the gonio-puncture at the 9-o'clock position there was a peripheral anterior synechia. Just under this synechia was an opacity in the lens. The tension was 20 mm. Hg.

On November 20, 1957, the total serum cholesterol level was 167 mg. percent. Between October 9th and December 6th, the tension ranged between 24 and 35 mm. Hg (Schiø:z), but after December 6, 1957, it remained within normal limits.

When the child was examined on April 9, 1958, the right eye was entirely normal. The iris was a light blue-gray color. The iris of the left eye was still thickened and the surface iris vessels were congested. The yellowish-brown color had not changed appreciably. The corneal diameter in the right eye measured approximately 12 mm. and in the left eye 12.5 mm. The left pupillary area appeared entirely clear. With a dilated pupil, however, it was noted that the entire central portion of the lens had been absorbed and there was a doughnutlike opacity of cortical and capsular material outside of the central four-mm. pupillary area. Ophthalmoscopic examination revealed the fundus to be entirely normal.

On May 12, 1958 the child was given a general anesthesia. The tension at that time measured 20.4 mm. Hg (Schiøtz) in the right eye and 17.8 mm. Hg (Schiøtz) in the left. Retinoscopic examination revealed a +0.75D. sph. refractive error in the right eye and +12.0D. sph. in the left eye. The iris in the left eye was normal or slightly thinner than normal and was slate gray in color (fig. 6). Gonioscopic examination showed the angle of the anterior chamber in the right eye to be entirely open. In the left eye the angle appeared open in every area except superiorly where it was somewhat shallow. The

area of the goniopuncture could not be seen.

The patient's photophobia and circumcorneal congestion cleared in March, 1958, and the eye has been entirely free of inflammatory signs since that time.

Discussion

The diagnosis of nevoxantho-endothelioma (juvenile xanthogranuloma) in the first case is open to question. However, the patient is included in this report because of the repeated spontaneous anterior chamber hemorrhages and the characteristic appearance of the lesion in the iris; that is, the yellow-brownish or salmon, diffuse, patchlike tumor of the iris. The biopsy of the iris showed cells that were compatible with histocytes in addition to inflammatory cells. These two observations suggested the possible diagnosis of nevoxantho-endothelioma.

It is interesting that the ocular lesion in the first case did not develop until the patient was three and one-half years of age. In the other reported cases this involvement has always been noted before six months of age. However, in the case of epibulbar nevoxantho-endothelioma reported by Cogan and his coworkers the lesion did not occur until the age of three and one-half years. Thus, it is not unreasonable to suspect that intraocular involvement also can occur at a later date.

In the second patient, the iris lesion was not biopsied. The skin lesions, however, were diagnosed as nevoxantho-endothelioma by a competent dermatologist, and Dr. Helwig reported that the histologic examination of the skin lesions was compatible with the diagnosis of nevoxantho-endothelioma.

The rationale for the use of X-ray therapy in uveal involvement and nevoxantho-endothelioma stems from several points. First, the similarity of the histologic picture of nevoxantho-endothelioma to the diseases known as reticulo-endotheliosis (eosinophilic granuloma, Schüller-Christian disease and Letterer-Siwe disease). It is not the purpose of this presentation to enter into a discussion of the relation of nevoxantho-endothelioma to the reticulo-endotheliosis. Crocker,[5] Lever,[6] and also Ormsby and Montgomery[7] note that this disease is probably a benign form of the reticulo-endotheliosis. Blank and his co-workers[1] mention that the only systemic manifestation of nevoxantho-endothelioma has been the intraocular involvement. Helwig and his co-workers[8] feel that juvenile xanthoma is a different entity from the reticulo-endotheliosis. In their examination of 53 cases with the diagnosis of juvenile xanthoma, only one patient was found to have systemic lesions. These involved the testis and lung.

The second reason for using X-ray therapy in ocular nevoxantho-endothelioma is that regression of the isolated lesions of eosinophilic granuloma and of Christian-Schüller disease has been noted following doses of radiation between 600 and 700 r.[9-12] Thirdly, it is known that the skin lesions of nevoxantho-endothelioma usually disappear spontaneously even after they have been present for a period of two to three years.

It was, therefore, reasoned that since in all previous cases of uveal involvement of nevoxantho-endothelioma, the patients had either lost their eyes from secondary glaucoma or had had a marked reduction in visual acuity, if X-ray therapy would cause the iris lesion to subside rapidly, the secondary glaucoma might be brought under control and the eye saved, even though the X-ray therapy might produce an irradiation cataract.

The first child has now been followed for approximately five years since the X-ray therapy was used. Only mild peripheral anterior subcortical lens opacities are noted. This may well be due to the relatively small amount of irradiation that reached the lens due to the extremely soft irradiation that was used.

The dose of X-ray therapy used in the second case was obviously cataractogenic. Merriam and Focht[13] have clearly pointed out that a single dose of 200 r to the lens is sufficient to produce a stationary lenticular opacity. A dose of 500 r in a single dose is enough to produce a progressive cataract.

While the irradiation used was not given as a single dose, the treatments were given over a period of only five days which is almost equivalent to a single dose of irradiation therapy.

The question as to whether the cataract in this second case was due to the irradiation or was due to the goniotomy is more difficult to determine. The lenticular opacity in this child was first noted approximately one month after irradiation. The area of opacity was located in the 3-o'clock meridian just under the area of the goniopuncture.

The question as to whether these two eyes were saved because of irradiation therapy or because of some other factor cannot be answered at the present time. It should be mentioned, however, that there are approximately 12 eyes with this disease that have been collected by Dr. Theodore Sanders,[14] all of which have been enucleated because of a suspected intraocular tumor and because of intractable secondary glaucoma. It is possible that, if a correct diagnosis had been made in these cases, they could have been followed and in some eyes the lens lesion would have regressed spontaneously. This, however, is mere speculation. The second point which should not be overlooked, is the fact that in both of the children here reported cortisone therapy was used. An apparent response to this form of treatment has been noted in Schüller-Christian disease.[9]

The ocular picture of uveal involvement in juvenile xanthoma is so characteristic that this diagnosis should be strongly suspected when a child is seen who has had a history of repeated spontaneous anterior chamber hemorrhages and diffuse thickening or yellow-brown or salmon patchlike lesions in the iris. If the pupil can be widely dilated, involvement of the ciliary body may be noted. The aqueous ray is usually positive and fine to moderate size keratic precipitates may be present on the posterior surface of the cornea. The onset of the lesion usually occurs during the first six months of age but in one case reported here it appeared in a child aged three and one-half years. Biopsy of the iris reveals a variety of inflammatory cells and numerous histiocytes. The diagnosis is greatly strengthened if xanthomas can be found on the skin and if one of the lesions can be biopsied for histologic study.

Once the diagnosis of nevoxantho-endothelioma has been made, it is suggested that the child be placed on topical and systemic cortisone therapy. If secondary glaucoma develops, an attempt should be made to control the tension with Diamox and miotics or mydriatics. If the glaucoma cannot be controlled and the eye shows early evidence of enlargement, then X-ray therapy should be given. A single dose should not exceed 200 r to the lens, and preferably should be in the neighborhood of 150 r lens dose. If more X-ray therapy is needed, it may be given at intervals of two to three weeks. More than 500 r should not be used unless it is obvious that the eye cannot be saved unless the larger dose of X rays is administered.

Summary

Two cases of uveal involvement of nevoxantho-endothelioma have been reported. In both instances the eye has been saved following therapy. In one eye, the child developed an irradiation cataract which absorbed, leaving a completely clear pupil. The clinical picture of this lesion has again been emphasized and various possible forms of treatment have been discussed.

The Johns Hopkins Hospital (5).
Walter Reed Army Hospital (25).

---

*After this communication was submitted for publication, a report of an eye treated with X rays for nevoxantho-endothelioma was published by Dr. Charles C. Hedges, Jr. (Am. J. Ophth., **47**:683 [May] 1959).

References

1. Blank, H., Eglick, P. G., and Beerman, H.: Nevoxantho-endothelioma with ocular involvement. Pediatrics, **4**:349, 1949.

2. Maumenee, A. E.: Ocular lesions of nevoxantho-endothelioma (infantile xanthoma disseminatum). Tr. Am. Acad. Ophth., **60**:401, 1956.
3. Newell, F. W.: Nevoxantho-endothelioma with ocular involvement: A report of two cases. Arch. Ophth., **58**:321, 1957.
4. Cogan, D. G., Kuwabara, T., and Parke, D.: Epibulbar nevoxantho-endothelioma. Arch. Ophth., **59**:717, 1958.
5. Crocker, A. C.: Skin xanthomas in childhood. Pediatrics, **8**:573, 1951.
6. Lever, W. F.: Histopathology of the Skin. Philadelphia, Lippincott, 1949, ed. 1, p. 354.
7. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin. Philadelphia, Lea, 1954, ed. 8, p. 745.
8. Helwig, E. B., and Hackney, V. C.: Juvenile xanthogranuloma (nevoxantho-endothelioma). Am. J. Path., **30**:625, 1954.
9. Avery, M. E., McAfee, J. G., and Guild, H. G.: The course and prognosis of reticuloendotheliosis (eosinophilic granuloma, Schüller-Christian disease and Letterer-Siwe disease): A study of 40 cases. Am. J. Med., **22**:636, 1957.
10. Willi, H., and Müller, J. H.: Successful roentgen therapy of a severe case of Hand-Schüller-Christian disease. Helvet. Paediat. Acta, **5**:212, 1950.
11. Radding, M. B.: Schüller-Christian disease after x-ray therapy, living and under observation 11 years. Radiology, **24**:591, 1935.
12. Dundon, C. C., Williams, H. A., and Laipply, T. C.: Eosinophilic granuloma of bone. Radiology, **47**:433, 1946.
13. Merriam, G. R., Jr., and Focht, E. F.: A clinical study of radiation cataracts and the relationship to dose. Am. J. Roent., **77**:759, 1957.
14. Personal communication.

BETA RADIATION IN OPHTHALMOLOGY*

Indications, technique and complications

Brendan D. Leahey, M.D.
Lowell, Massachusetts

One of the most important recent advances in ophthalmology is the development of beta-ray therapy. Since 1948 we have treated at the Massachusetts Eye and Ear Infirmary and in our office group 320 human eyes with beta radiation from a radium-D applicator, and from the experiences and mistakes of this series much worthwhile information may be gleaned. Of special interest has been the occasional occurrence of ulceration of the cornea several years after apparently successful radiation.

Types of radiation

For better understanding of these rays it might be profitable to review briefly certain basic facts in radioactivity.

The atom is composed of a center or nucleus and a number of tiny electrons which move around the nucleus in certain fixed orbits. The arrangements of these rings or orbits gives rise to definite properties of the elements and determines their chemical behavior. The electrons carry a negative charge. The nucleus is made up of neutrons and protons. The protons have positive charges which exactly balance the electron charge, and the neutrons carry no charge.

Certain atoms tend not to retain their stable nucleus and outer electron form, and undergo a kind of nuclear re-arrangement in which radiations or particles are emitted. Elements that undergo this change are termed radioactive. The farther away an electron is from the nucleus the more potential energy it carries, and when an electron moves from an outer orbit to an inner one, it emits energy in the form of radiation; conversely, when moving from an inner orbit to a more remote one, it absorbs energy.

There are four distinct types of radiation associated with radioactive materials.

1. Alpha rays, are positively charged particles, travel at a speed of 10,000 to 20,000 miles per second, and have a range from 3.0 to 9.0 cm. in air. They have no penetrating power and can be stopped by even a thin sheet of paper, hence have little therapeutic use.

2. The beta rays are also definite particles, with negative charges. They are actually electrons. They normally travel in a straight line at about the speed of light but will swerve from their path if exposed to a magnet. There is considerable variation in penetration power of the so-called beta group, the less penetrating rays being called soft and the more penetrating one hard rays. In general, they

* Presented before the New England Ophthalmological Society, March 19, 1958.

can travel about 9.0 to 10 cm. in air, up to 1.0 cm. in tissue, and are stopped by one to two mm. of silver or lead.

3. Gamma rays, unlike alpha and beta rays, are not definite particles but are electromagnetic or wave-form radiations. Their wavelength is very short and their penetration is very much greater. Certain gamma rays can penetrate up to 10 inches of steel and these are used industrially in the detection of metal flaws.

4. Recently, a fourth type of radiation has been recognized, neutrons. Like beta particles the neutron is a mass, but it has no charge. It is released from the nucleus by bombardment with high energy particles, such as protons or deutrons and is an important factor in atom bomb injuries. Some of these fast neutrons can penetrate one inch of lead, and they can cause marked tissue damage. So far, they have been used medically only for research projects.

Sources of beta radiation

At present there are five possible ways of administering beta radiation: X rays, or by use of applicators containing radium, radon, radium D, or an isotope such as strontium 90.

1. X rays. Soft beta rays can be administered very effectively by certain X-ray machines. X rays of 10 to 20 kv. give results about similar to a radon applicator. The Philips' contact therapy machine which produces X rays of 44 kv. would produce somewhat deeper effects and cannot be safely used on the anterior portion of the eye. The ordinary Grenz ray machine produces rays of 8.0 to 12 kv. and therefore its clinical effects are relatively superficial compared to those of radon, radium, and strontium 90, but are similar to those of radium D. The great difficulty with X ray is that it is practically impossible to limit treatment to a definite small area of the cornea due to the motion of the eye and consequent difficulty in properly centering the lead diaphragm. X rays on the anterior eye ball should be reserved for cases where the entire cornea or similar large areas need treatment and should be given only with a low voltage machine to avoid cataract formation.

2. Radium. Radium applicators as used by Iliff[1] contain 50 mg. of radium and have a flat rectangular active surface 6 × 12 mm. Besides the beta particles, radium gives off gamma rays which penetrate very deeply. Because of the relatively small amount of gamma radiation in comparison with the beta particles, however, it was felt by Burnham[2] and Iliff[1] that in the time interval required for beta treatment, the amount of gamma rays absorbed in the eye would be of little consequence.

3. Radon. Radon gas is collected in a vacuum glass tube from a solution of radium chloride. The alpha particles are completely absorbed by the thin layer of glass surrounding the radon. The beta particles penetrate the glass tubing and emerge through the five-mm. diameter open end of the applicator. In proportion to the beta output, radon gives out less gamma than the radium applicator, but the gamma is still a potentially objectionable factor.

Because of the gamma radiation, it is necessary to use a rather awkward long handle on radium and radon applicators, and to avoid giving many treatments over a short period of time for the operator's own safety.

For the same reason a radon applicator must also be stored in a lead container with walls at least one inch thick. Another disadvantage of the radon is its short half-life, 3.5 days, and the fact that a radon producing plant must be available.

Radon applicators have the advantage of a higher output of energetic beta particles, so the treatment time may be reduced to 40 seconds as compared to six minutes with the radium or radium D plaque.

4. Radium D. Unlike radium and radon, radium D-E emits almost pure beta radiation with an average beta energy of 0.34 mev. (million electron volts) and a maximum of 1.17 mev.

Tests[3, 4] at the Massachusetts Institute of Technology and other institutions show that the amount of gamma radiation given off is infinitesimal. The radium D applicator has a round treatment surface 5.6 mm. in diameter. The standard applicator contains 10 cm. of radium D-E. I used one of these in 1948, but because of the slow treatment time, soon had one made up with 20 mc. (fig. 1). Incidentally, when the amount of radium is doubled in this applicator, there is only a 50-percent increase in the effective output because of even greater self absorption of the beta particles within the increased radium-D mass. This stronger applicator has been extremely satisfactory. Because of the absence of gamma rays, radium-D treatments may be given with the hand only one or two inches from the tip of the applicator, instead of the 10 inches advised for radon and radium ones. One mm. of lead stops

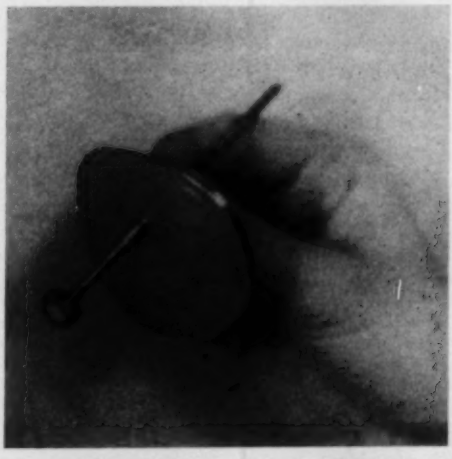


Fig. 1 (Leahey). Radium-D applicator and shield.

soft beta rays, so that a thin metal shield in front of the hand is used as additional precaution.

Where treatment is prolonged, a mechanical holder is advantageous. The Stevenson holder,[5] which attaches to the speculum, is rather difficult to adjust and with it slight motion of the speculum is enough to allow the applicator to rub on the cornea. I designed one[6] in 1941, consisting of a malleable wire (fig. 2a) which slides into holes in an eyeglass frame or a headband. The wire is bent into place over the desired area of the cornea and the fine adjustment is made on an easily turning screw.

5. Strontium 90. In 1950, Friedel, Thomas and Krohmer[7] developed the strontium applicator. The useful beta particles come from the equilibrium product, yttrium 90. As in the case of the radium D, strontium 90 has no gamma rays but the beta has much more penetration than that of radium D. It has a half-life of 25 years and it costs approximately one fifth as much as the 20 mc. radium D applicator. The standard applicator on the market has a diameter of 7.8 mm. which is too large for many eye treatments. Special smaller strontium 90 applicators can be made, however, and Hughes has used one five mm. in diameter.

Fig. 2a (Leahey). Mechanical holder for radium-D applicator. A malleable wire slides into holes in an eyeglass frame or headband. This wire is bent into place over the cornea and the fine adjustment is made on an easily turning screw.

Penetration of beta rays

In 1951, Krohmer[8] of Western Reserve published some very important work in regard to the penetration in tissue of the beta rays from these various applicators (table 1).

Krohmer's studies show that the radium D beta is almost completely absorbed in the first two mm.; whereas, a considerable percentage of beta from the other applicators is still present at four mm. with the greatest penetration being that of the strontium 90. Incidentally, a low-voltage X-ray machine, such as the Philips unit, produces at contact, and without added filter, a 23 percent surface dose at 10 mm!

Since the equator of the lens may be only three mm. from the corneal surface at the limbus, these figures indicate that radium D is the only one of these sources which does not allow considerable radiation to reach the lens.

Measurement of radiation

X rays are measured in roentgens. The roentgen is based on the ionization produced in a fixed mass of air (1.0 cc.) as a result of incident X rays, and is not concerned with the effect in tissue. Since a great deal of biologic data concerning the use of X rays is in terms of roentgens, attempts have been made recently to utilize this unit or one very closely related to it for the measurement of radiation dosage of all types, whether from a source outside the body or from within the body, such as from injected P^{32}. This has resulted in a concept of an equivalent roentgen as a measure of ionization in tissue, or more directly, of energy absorbed in tissue. Thus was born the new measuring unit, rep (roentgen equivalent physical). This unit is based on the energy absorbed in tissue instead of in air.

Because of the many factors involved, there is no way to translate roentgens back and forth into rep, but judging from the surface erythema dose (150 r or 3,000 rep) 1.0 r of low voltage radiation (8 to 12 kv.) has the equivalent surface skin effect of 20 rep of radium-D beta.

Unfortunately, due to the variation in different

TABLE 1

Beta applicators: Percent of surface dose at various depths (Krohmer)

	0	1 mm.	2 mm.	3 mm.	4 mm.
Radium	100	16.9	7.6	3.7	1.8
Radon	100	31.	15.	8.	5.
Sr. 90	100	41.	18.	9.	6.
Radium D	100	10.	.9	—	—

applicators of the same type owing partly to the actual distribution of the radioactive material in the applicator, standardization appears to be poor. It is necessary therefore, to test each applicator by skin test and on living eyes to determine its actual clinical performance.

Since 1948, various authors have reported widely different doses in rep for effective treatment of corneal vascularization. Besides the individual variation in applicators, there is an even more striking reason for this discrepancy. The original 10 mc. radium D applicators were said by the manufacturers[4] to have an output of 200 rep per minute; and a 20 mc. applicator would give 50 percent more, or 300 rep per minute. This "200 rep per minute" value has been widely quoted[9] and even included in applicator comparison tables, such as the excellent ones of Wilson[10] in 1952.

The method of calibration was changed markedly a few years ago and most applicators are now calibrated in an extrapolation chamber by the method of Krohmer of Western Reserve University.[8] My 20 mc. applicator is over 10 years old. It was calibrated twice in 1957 (by Tracerlab and by Technical Operations Inc.) and found to have an output of 1,200 rep per minute. This means that effective treatments which were 750 rep by 1948-1952 manufacturers standards were actually 3,000 rep by current standards. Obviously this 400 percent change has caused much misunderstanding and confusion in the interpretation of published results.

This, of course, is another reason why the actual clinical performance of each individual applicator must be carefully studied.

Nearly all authors recommend contact dosage for treatment of corneal conditions; but we find this causes irritation of the cornea, and have always held the applicator about one mm. from the cornea. Incidentally, Tracerlab measurements which assigned my radium-D applicator an output of 19.7 rep per second show this surface dose is reduced by one mm. of air to 10.4 rep; so treatment time must be correspondingly increased when the applicator is held one mm. from the eye.

In 1948, Canadian Radium and Uranium Corporation made a one-mm. silver fit-over shield (fig. 2b) for my applicator, with a 2.0 by 5.0 mm. oblong opening, for use on isolated vessels. It was felt that cutting down the effective diameter of the opening would introduce an important filter factor but this proved not so for this size opening at distances as short as one or two mm. Contact therapy with the one mm. thick filter in place gave essentially the same surface dose per mm. as the applicator without the filter held one mm. from the cornea. This was again confirmed by calibration tests at Tracerlab in 1957.

Conditions for which beta is indicated

1. Removal of corneal blood vessels

Removal of corneal blood vessels has long been a problem in ophthalmology, especially in cases needing keratoplasty. A heavily vascularized scar was formerly a hopeless case for corneal transplantation. Some of these vessels can be closed by means of cautery applied to the vessels at the limits for two mm. I have done a very large number of these but, in general, my results were not satisfactory. Nine out of 10 of the vessels soon reopened. Superficial keratectomy is helpful when the vessels are large and superficial but again the results of stripping are disappointing. Radiation is the most effective method. (fig. 3). As radiation works well only on small vessels and new capillaries, the largest ones should still be treated by preliminary stripping, or by cautery peritomy, immediately after the first radiation treatment.

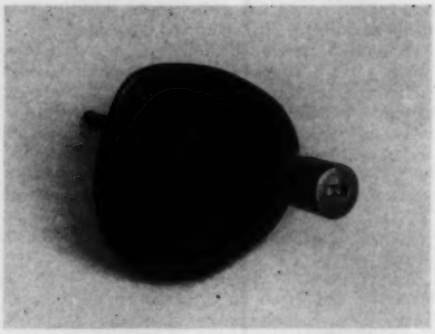


Fig. 2b (Leahey). Silver shield for radium-D applicator with a 2.0 by 5.0 mm. oblong opening for use on isolated vessels.

Due to the lack of penetration of radium D beta, some authors[11,12] consider it rather ineffective in treating corneal vascularization. Since 1948, my radium-D applicator has been used on several hundred eyes for corneal vascularization of many types, and in nearly all of these cases, the radium D proved extremely effective even with deep vascularization. For vessels in the posterior 25 percent of the corneas however, radium-D treatment time must be increased. Consequently, for these occasional cases more penetrating beta such as that from strontium 90 is advantageous. This greatly increases the danger of cataracts but also decreases the possibility of over treatment of the superficial corneal layers.

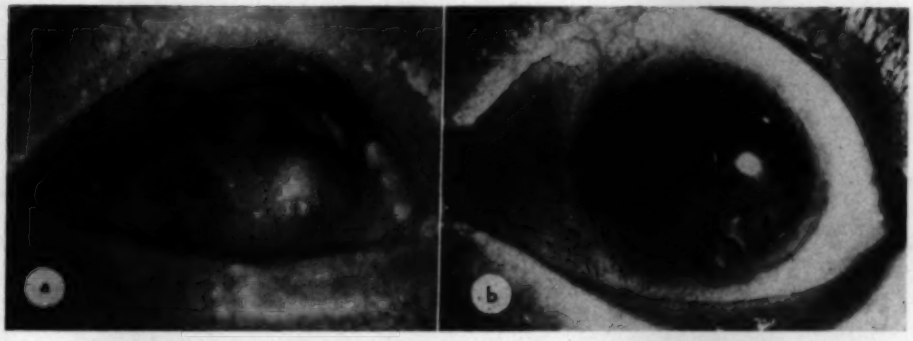


Fig. 3 (Leahey). A. G. (a) Marked corneal vascularization two years after a chemical burn. (b) Same cornea after 18,000 rep radium D beta. Vascularization has almost entirely disappeared and the cornea is much less opaque.

When there is extensive thick pannus of the cornea, a superficial keratectomy is done, and the conjunctiva and the scar tissue is resected for four mm. back of the limbus. The sclera is scraped bare and free of vessels in much the same manner as when transplanting a pterygium (fig. 4). It was formerly thought that complete recession of the conjunctiva all around the limbus, leaving the sclera bare, would cause interference with corneal nutrition and possible serious corneal damage. In 1947, however, Lombardo[13] showed that this method was often helpful in removal of extensive pannus in trachoma and caused no damage to the cornea. I tried this method on a few cases, but did not find it effective until it was also combined with radiation.

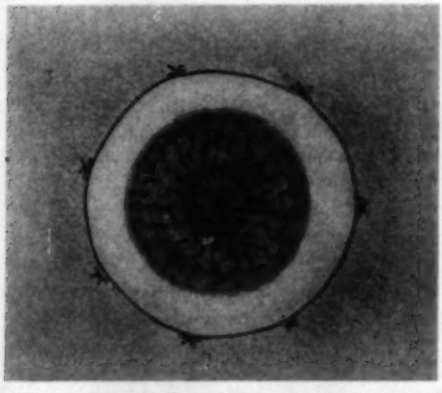


Fig. 4 (Leahey). Diagram of complete superficial keratectomy with resection of conjunctiva and scar tissue four mm. back of limbus preliminary to beta radiation for complete corneal pannus.

The cut edges of the conjunctiva are held in position by four silk sutures passed through episcleral tissue. Three days later beta radiation is started before the vessels have time to grow in again (fig. 5).

When treating chemical burn cases, corneal stripping or radiation alone should not be used until the eye is free from marked inflammation. This often means waiting for two years or more after the original burn. If beta is administered while the eye is still very inflamed, it would be of no value as the continued irritation causes continued growth of new blood vessels. If the full quota of beta is thus applied uselessly it would not be available at the later proper date and a transplant could probably never be done.

2. Rosacea keratitis

Beta radiation has been a spectacular success in treating rosacea keratitis (fig. 6). The vessels are superficial and respond readily to beta. With the decrease of vascularity in the cornea, there is also a tremendous decrease in the tendency to develop active keratitis. In general, the beta radiation should be applied between the keratitis attacks. Occasional eyes, however, are never free from keratitis. In these desperate cases, the radiation may be given while the eye is

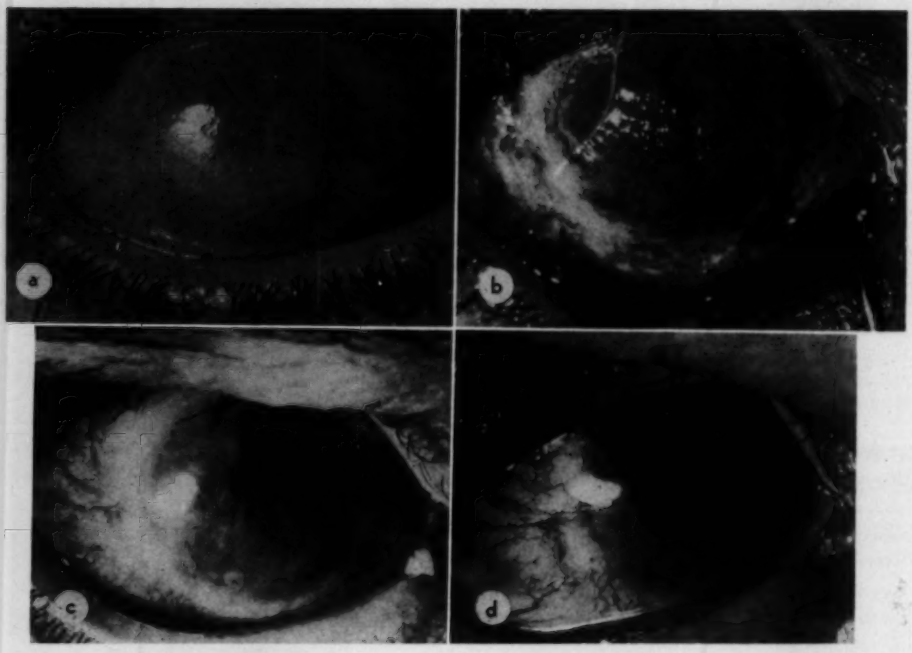


Fig. 5 (Leahey). J. M. (a) Dense pannus of 10 years' duration. Vision, light perception only. (b) Four days after complete superficial keratectomy and recession of conjunctiva and scar tissue four mm. beyond the limbus. Beta was started on this day. (c) Same eye four months after keratectomy and beta. Cornea is almost avascular and moderately translucent. It is now suitable for a graft. (d) Same cornea 10 months after keratectomy and beta and six months after a five-mm. penetrating graft. Eye is quiet and vision is 20/60. Left eye has also had similar treatment and result.

inflamed and many of these also have good results. One such patient seen in our clinic at the Massachusetts Eye and Ear Infirmary had extreme active rosacea keratitis of both eyes continuously for several years with complete disability. Following beta, he has been free of inflammation for three years with considerable restoration of vision.

3. Vernal conjunctivitis

This is the third condition for which beta radiation is almost a specific cure (fig. 7). It should be used only on eyes with prolonged history of vernal conjunctivitis and no adequate relief from adrenalin solution or local steroids.

In order to reduce the amount of radiation necessary, the larger follicles are trimmed off with scissors at the time of the first beta treatment. The follicles should not be trimmed closer than 0.5 mm. from the lid surface to reduce possible lid damage. The beta is applied as a spray treatment three or four times at one-week intervals with approximately 1,500 rep being delivered to any one area on the lid for a total of 6,000 rep in four treatments.

Of the vernal cases seen in New England, 90 percent are the palpebral type and only 10 percent have bulbar involvement. The results have been wonderful in both types, however. In several early severe cases only one eye was treated in order to evaluate the results more accurately. In three such cases with a long follow-up, each had almost complete freedom from symptoms in the treated eye

but continued vernal irritation in the other eye two to three years later. At the end of this time the other eyes of these same patients were also treated with beta with good results.

Where a small amount of radiation is given, there is frequently partial recurrence of the vernal symptoms after three years; but it should be possible to re-treat these once or twice in subsequent years, if necessary, without danger of radiation damage as the swollen follicles are far more sensitive to radiation than is the normal lid tissue.

4. PTERYGIUM

a. *Primary pterygium.* Between 1948 and 1950, we treated with beta, for our own group or for the Eye Clinic at the Massachusetts Eye and Ear Infirmary, 20 patients with simple primary pterygia (fig. 8). In every case, the treatment gave a clinical cure. The pterygia treated varied from tiny thin ones to large fleshy ones encroaching four mm. on the cornea. We soon found the amount of scar tissue formed was in direct proportion to the size and thickness of the pterygium. The fleshy pterygia left a dense white scar over the treated area with a poor cosmetic result. Since this cosmetic result is far inferior to that obtained with a McReynolds transplant, we have discontinued beta for primary cases. Because of the poor cosmetic result and because of the possible dangers of beta, I believe the use of beta on primary pterygia is, at present, completely unjustifiable.

b. *Recurrent pterygium.* If a pterygium has been satisfactorily transplanted once and recurs, it has been the experience of most surgeons that it will probably again recur. For these recurring pterygia, we have found beta radiation a specific cure (fig. 9). The pterygia are again transplanted and three days later, beta is started over the denuded area and the adjacent area just peripheral to the limbus. We have treated approximately 60 of these cases. We have no follow-up on many of the patients referred from physicians in other states, but to the best of our knowledge we have not had a recurrence on any patient so treated. I believe recurrent pterygia should be considered the number one indication for radium-D treatment.

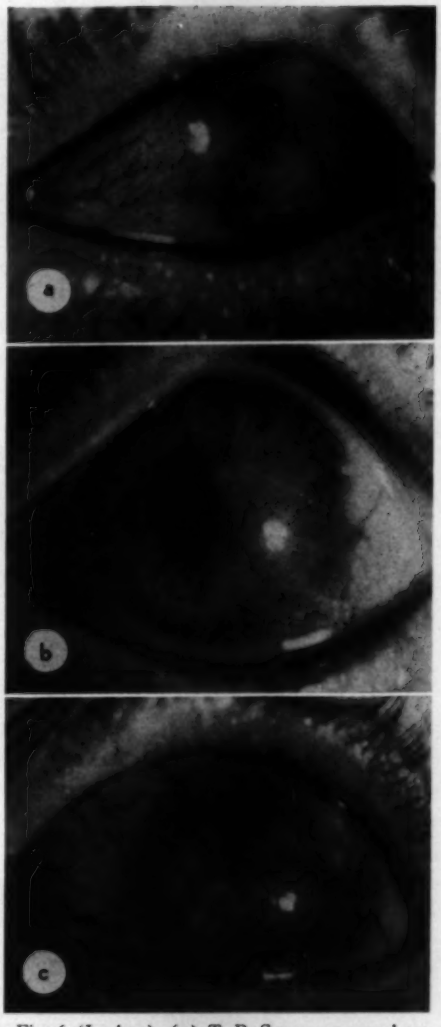


Fig. 6 (Leahey). (a) T. B. Severe rosacea keratitis. (b) Same eye. Complete disappearance of corneal vessels following beta. (c) M. H. An extreme rosacea keratitis with continuous activity for several years despite treatment. This eye improved promptly after beta and remained inflammation-free for the past three years.

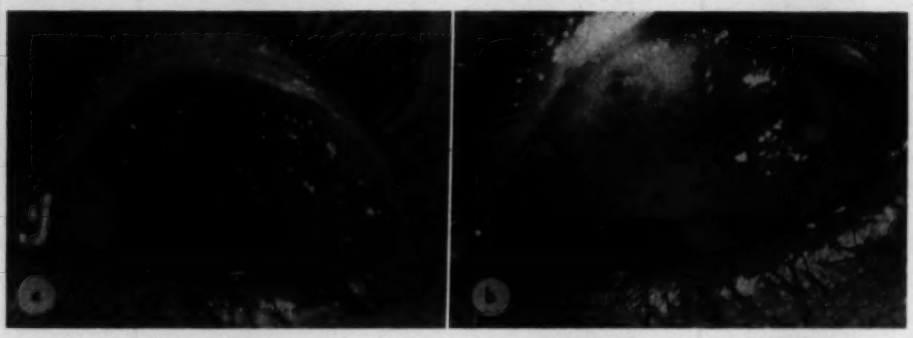


Fig. 7 (Leahey). C. F. (a) Severe vernal conjunctivitis with extreme follicles. (b) Same eye two years later is essentially symptom-free following excision of follicles and beta radiation. Opposite eye, however, although originally less severely involved, has become much worse.

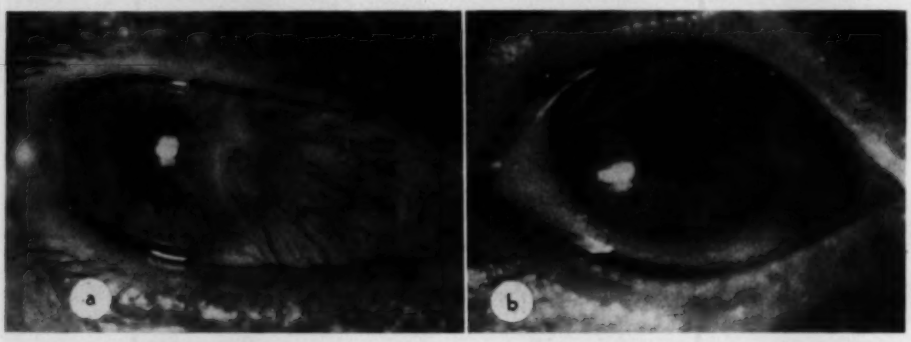


Fig. 8 (Leahey). A. F. (a) A typical primary pterygium. (b) Same pterygium avascular and inactive following 15,000 rep radium D-beta. Since radiation leaves a more dense white scar than excision, it is not recommended for the usual primary pterygium.

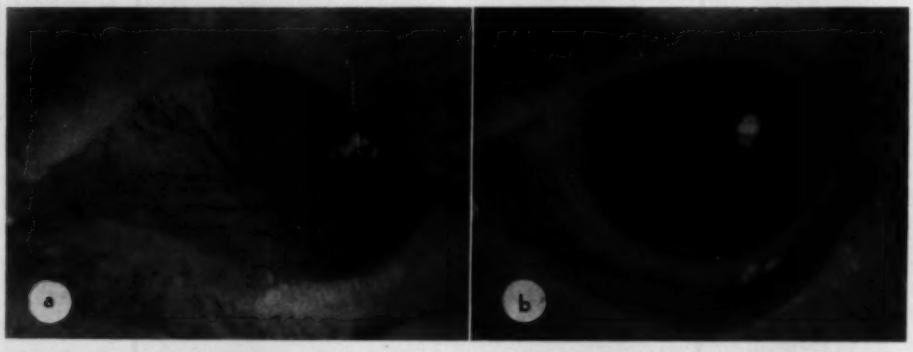


Fig. 9 (Leahey). M. R. (a) Actively growing recurrent pterygium. This has had two previous McReynolds transplants. (b) Complete cure one year after a new pterygium transplant and beta radiation. Beta is extremely effective in treatment of recurrent pterygium.

5. Chronic sclerokeratitis

Some cases of chronic sclerokeratitis, both of tuberculous and of nonspecific type, have shown dramatic improvement following beta-ray therapy after months of the usual treatment had been unsuccessful. Since the beta is not as successful for sclerokeratitis as for the pathology involving vascularization, already mentioned, beta should be tried only when other treatments prove unsatisfactory.

6. Interstitial keratitis

Several authors have reported this to be favorably influenced by beta radiation. Since the systemic and topical steroids take most of the inflammation from interstitial keratitis and greatly decrease the vascularity, I feel that beta radiation for acute interstitial keratitis is at present contraindicated.

7. Other forms of corneal inflammation

Judging from the effect of our applicator on 12 cases of chronic dendritic keratitis and disciform keratitis, beta radiation is of no value for herpes simplex infection. We have avoided treating pemphigus cases, but results elsewhere are not encouraging. Radiation seems also to be of no help for pyogenic ulcers.

8. Corneal scars

There have been a number of reports in the literature of corneal scars being less marked after beta radiation. These reports are practically all from radiologists rather than from ophthalmologists, and in some of the acute cases, the so-called scar was undoubtedly an opacity from active keratitis. There is no physiologic reason why an old inactive corneal scar should decrease with radiation. On the contrary, there are many reasons why it could become more marked. Radiation is contraindicated.

9. Hemangiomas on bulbar conjunctiva or unsightly dilated capillaries

In general, these are best treated by excision, diathermy occlusion, or carbon dioxide snow. The larger ones on the lids respond to injections of sclerosing solution (five-percent sodium morrhuate). When there are many fine vessels in the bulbar conjunctiva and episclera, however, a combination of diathermy and radium D-beta does give an excellent cosmetic effect.

10. Granuloma

In 1949, I used radium D experimentally on three eyes with exuberant granulation tissue at the site of strabismus surgery. The results were excellent but it is actually far simpler and safer merely to snip off the granuloma with scissors, and I consider such excision the treatment of choice.

11. Epithelial downgrowth in anterior chamber

A number of these cases at the Massachusetts Eye and Ear Infirmary have been treated with X rays but the results are questionable. Results elsewhere appear equally dubious. Since the radium-D applicator lacks adequate penetration it would be of no value for this condition even if radiation were effective.

12. Epithelioma

Radium D is again of no value because of its lack of penetration. Radium, radon, and strontium 90 applicators would do a much better job. In general, however, epitheliomas are treated better by X rays since the area to be covered is often wider than the applicators, and since greater penetration is usually desired. Since I have been primarily interested in corneal vascularization, I have referred all epitheliomas not treated surgically to roentgenologists (fig. 18).

Effect of radiation on tissue

In order to understand the complications, we must first understand the effect of radiation upon the tissue. Ionizing radiation consists of either electromagnetic radiation (gamma rays) or particles in motion, such as beta rays or electrons. Either type of

radiation may completely transverse any particular segment of the matter or may be absorbed. Much of the energy absorbed is the result of a knocking out of atomic electrons from their orbits. These, in turn, collide with other orbital electrons and displace them. Thus, displaced atomic electrons or beta particles play a very important part in the distribution and absorption of energy and tissue. Energy absorption in any particular tissue is an important consideration and the biologic effect depends mainly upon this energy absorption rather than on the source of the energy. In the final analysis it matters little whether the energy absorbed came from the radioactive isotope administered internally, gamma radiation from a cobalt course, X rays, or a beta-ray applicator. Ionizing radiation alters the molecular structure of cellular and extracellular fluids, resulting in new compounds that may be toxic to the cell.

Radiation never stimulates. Occasionally, under certain conditions an apparent secondary stimulation occurs as a result of the depression or destructive effect of radiation and the response to these effects. With the beta applicator, these tiny particles or electrons are actually driven into the tissue at the speed of light, causing changes in the nucleus and the cytoplasm of the tissue cells. Large doses cause destruction and even necrosis. The susceptibility of cells to irradiation varies during their lifetime, the cells being most sensitive during growth and mitosis. Of special importance in our work, is the high degree of sensitivity of the endothelial cells lining the blood vessels. The thin endothelial cells swell to bulging proportions and there may be temporary dilatation of the vessels and diapedasis. Later there is proliferation of fibroblasts and occlusion of the lumen. The effect is far more marked on young blood vessels. Connective tissue response takes place concomitantly with cell destruction. Excessive doses, therefore, besides leading to destruction of the blood vessels, may actually lead to increased scarring of the cornea.

Clinical course of treated case

For the average case of corneal vascularization, five, five-minute radium-D treatments (3,000 rep each) are given at one-week intervals for a total tof 15,000 rep. For fine superficial vessels 11,000 rep may be enough. The applicator is held one mm. off the eye. Under the slitlamp the corneal vessels appear to undergo an obliterative endarteritis. They get smaller in caliber, darker in color, and frequently show little hemorrhages along their course. Then short sections of the vessel disappear completely. The picture is usually not complete for three months after the last dose has been given.

Complications

A. Effect on the lens

Radiation cataracts have been recognized since 1897 with latent periods reported varying from three months to 12 years.[14] "The typical early clinical picture in man is that of a ring-shaped granular opacity in the region of the posterior capsule. Later the subcapsular cortex becomes speckled with minute snow-flake opacities. A mature cataract with liquefaction of the cortex can develop. The lesion need not be progressive and arrest may occur at any stage depending on the dose."[15]

Extensive studies on animals and humans, however, (Cogan, [16] Leinfelder,[17] von Sallmann,[18] Putenney and Shoch[19]) show that the initial damage is done to the epithelial cells at the equator of the lens. Leinfelder found the injuries in proportion to the mitotic index of the epithelium and studies of the mitotic index of the epithelium show it to be zero at the anterior pole and increasingly higher as the equator is approached.

Putenney and Shoch[19] found radiation cataracts in rabbits developed at different degrees depending on the extent and location of radiation.

Mature cataracts were produced only in eyes that received total irradiation of the whole lens. The radiation cataracts in rabbits were characterized by peripheral changes consisting of vacuoles or granules or both,

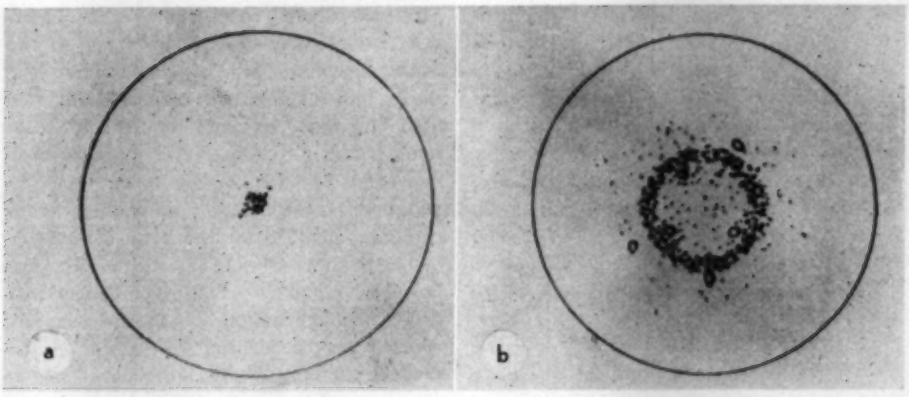


Fig. 10 (Leahey). Diagrammatic representation of early clinical appearance of radiation cataracts (after Cogan). (a) Early opacity in the posterior pole. (b) A later stage, showing the characteristic doughnut silhouette.

and these changes were confined to the subcapsular cortex. Their incidence was closely related to radiation directed to the equator of the lens. They found only 15 percent developed opacities when radiated through a central opening in the lead filter, but 100 percent developed cataracts when the periphery was radiated.

Cogan[16] thinks damage to the equator cells would be sufficient to prevent their full and normal differentiation. Some of these cellular changes may be looked upon as the results of abortive attempts to form lens fibers. These abnormal cells migrate or are pushed toward the posterior pole between the cortex and the capsule where they form the characteristic opacity of early radiation cataracts (fig. 10).

In 1955, McDonald, Hughes, and Pfeiffer[20] reviewed 73 radon-treated eyes in which the cornea was sufficiently clear to allow study of the lenses and in which the pupils could be widely dilated. Of these, 45 had definite radiation opacities and vacuoles. Thirteen had questionable opacities, 15 had none. The changes were in every respect similar to those seen in rabbit experiments, usually granules and vacuoles in the treated area with the base at the equator and the apex treated directly posteriorly. The earliest opacities seen were after 29 months.

They also concluded that, in general, rabbit lenses are four times more sensitive to beta radiation than the human lens and the lens tolerates about 10 times the beta dose when applied to the center of the cornea as when applied over the limbus.

B. Effect on conjunctiva, cornea and sclera

1. *Transient irritation.* There is usually slight irritation for a day or two from a combination of many factors including the actual radiation and the fact that the eye has been anesthetized and probably mildly traumatized by use of the lid speculum. This irritation is usually imperceptible, or at most, causes only slight inconvenience.

2. *Subacute irritation.* Some cases have a more marked irritation and ciliary injection with a slight ache in the eye for two or three days up to two or three weeks. This occurs in about 20 percent of our corneal cases and usually only after the third or fourth treatment when there is a greater cumulative effect from the radiation. If the irritation is marked, further treatment should be postponed or omitted. Occasionally, slight irritation persists for as long as two months.

3. *Telangiectases.* After prolonged treatment to conjunctiva, scarring and abnormal whiteness of the conjunctiva and episclera

may result as after-radiation to skin. About one year later such an area may occasionally develop one or two very tortuous irregularly dilated blood vessels like the telangiectases of heavily treated skin areas (figs. 15c and 17a. On rare cases with extensive heavily vascularized scars, slight telangiectases have also occurred on the cornea. In general, if telangiectases do not develop within 18 months they usually do not appear.

4. *Keratinization of the conjunctival epithelium.* This has been reported by Merriam[21] following doses of 5,000 to 10,000 rep. When the mucous membrane in the upper palpebral conjunctiva is converted to a keratinized epithelium, this roughened surface moving over the cornea may produce a punctate keratitis. This results in a severe chronic irritation of the cornea and treatment is relatively ineffective. This condition is unfortunately permanent. We have experienced no unpleasant sequelae in our own vernal catarrah series.

5. *Chronic irritation and ulceration.* If grossly excessive radiation is given, such as experimentally on rabbits, the eye may remain slightly congested for long periods and three or four months later an actual slough will develop on the cornea. This may perforate, or it may heal in another three or four months.

Experimentally, corneal ulcerations were reported by Wilson[10] following strontium 90 beta radiation of rabbits' corneas of 35,000 rep. In these eyes, the ulceration was present on the average from the 94th to the 178th day. The earliest ulceration occurred on the 28th day after exposure to 80,000 rep and the latest ulceration occurred on the 181st day after exposure of 40,000 rep.

In our series of radium D-beta treatments to human eyes, five eyes showed continued marked irritation and ciliary injection for months following treatment. Each of these cases had extremely dense corneal scars and had been subjected to superficial keratectomy followed by a total of over 18,000 rep in five doses one week apart.

In nonradiated cases, the average superficial keratectomy heals over in one to two weeks depending on the area covered and shows only moderate irritation during that time. In most of our keratectomy cases treated with radiation rather marked injection persisted for from one to three months and there was still some faint staining of the cornea a month after the keratectomy.

The five unfortunate cases described here, however, remained markedly inflamed with delayed epithelization of the cornea. All showed very superficial staining or ulceration of the cornea after periods of one to four months with marked redness, sensitivity to light, and considerable "deep ache" in the eye. Three of the eyes showed considerable inflammation for several months after healing and again had superficial ulceration of the cornea at intervals for one to six years after treatment. All eventually healed. Due to the irritation of the eye, new vascularization occurred and not one of these eyes was ever suitable for a corneal transplant.

The following case is typical of this group:

F. Z. In March, 1950, this 40-year-old man suffered a severe ammonia burn of the right eye and developed a heavily vascularized thick pannus (fig. 11a). Vision was light projection only. In May, 1951, a superficial keratectomy was done with excision of scar tissue around the limbus for three mm. A total of 51,000 rep was given to the cornea and adjacent sclera with a maximum of 18,000 rep to any single area.

The eye remained irritable, slightly injected, and rather light sensitive for six months; and during most of this time there was faint corneal staining (fig. 11b). In October, 1952, 16 months after the last beta treatment, a large bleb appeared on the central cornea. This ruptured later leaving an indolent corneal ulcer. The edges were rather clean and sharply defined. This ulcer healed in six months but, at intervals for the next six years, the eye was intermittently inflamed with occasional slight ulceration. A new pannus formed which was worse than the original one (fig. 11c). This cornea became completely unsuitable for transplantation.

This patient's opposite eye had also been burned and had a less complete pannus with very tiny vessels. This eye had no keratectomy but did have 18,000 rep administered to each of three areas. Convalescence was quiet and uneventful. Most of the vessels cleared and vision improved from 6/200 to 20/70.

Ulceration of tissue occurring one to four months after overradiation has also been reported[21] after X-ray therapy for malignancy around the eye and following radium and strontium 90 radiation of the sclera. It should be remembered, however, that the same amount of beta radiation that was used on the five eyes just described has been very successful on a large number of other eyes.

6. *Late ulceration of the cornea.* As already mentioned, it is generally realized that overradiation of the cornea may lead to ulceration starting about one to five months after the radiation therapy. Due to the short life span of rabbits, however, animal studies are not available on the effects of this radiation many years later. While late radiation necrosis has been described in most other body tissues, there is almost no mention in the literature of such ulceration appearing in the cornea several years after apparently successful uncomplicated beta radiation.

In my series, I have had six cases where the eye was apparently in excellent condition for one to eight years after beta radiation. At the end of this variable time severe indolent ulceration of the cornea suddenly appeared. It usually started as a superficial ulceration with a gray or white necrotic bottom and sharply defined edges that lacked any marked edema. In the worst cases, the crater would become progressively worse and deeper over the next three months and the slough at the bottom would disappear leaving a deep pit in the cornea with sharply defined edges almost perpendicular to the floor of this pit and no surrounding infiltrates. There was no evidence of healing around the edge. In one case, the ulcer perforated and was covered with a conjunctival flap. The others healed in from three to six months with considerable additional scarring.

CASE 1

J. F. This man (aged 60 years in 1949) had recurrent dendritic keratitis followed by severe disciform keratitis in 1930. There was a leukoma of almost the entire cornea containing a very dense plexus of small vessels deep in the stroma. Three

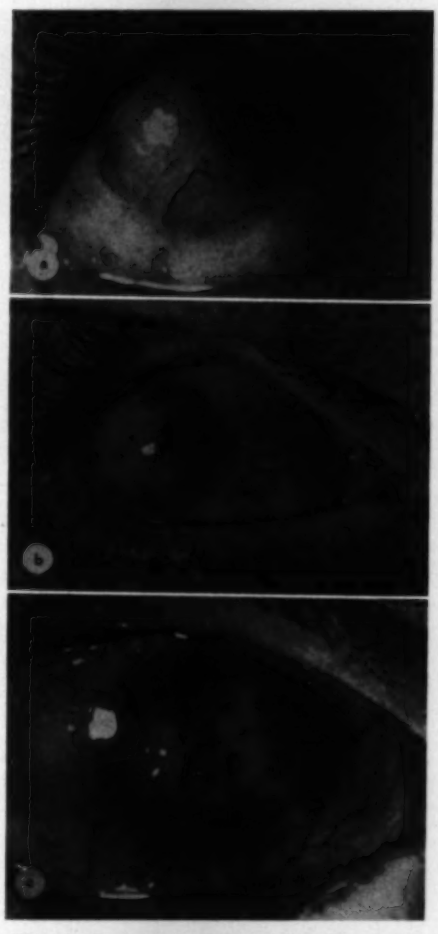


Fig. 11 (Leahey). F. Z. (a) A heavily vascularized thick pannus from an ammonia burn. Vision, light perception.

(b) Seven months after superficial keratectomy, resection of conjunctiva and scar tissue around limbus, and administration of 18,000 rep to each of several areas. The central cornea was clear of vessels, but the eye showed moderate irritation and a new pannus was growing in from the nasal side.

(c) Five years after beta. About 16 months after beta the first superficial ulceration appeared, lasting six months. The eye was free from inflammation for several months but again became inflamed and ulcerated on several occasions. Five years after beta there was a new pannus much worse than the original one. At the time of this picture, only the one-mm. dark area in the lower central cornea still stained. A wide circle of previous ulceration is obvious, however. This eye is unsuitable for transplantation.

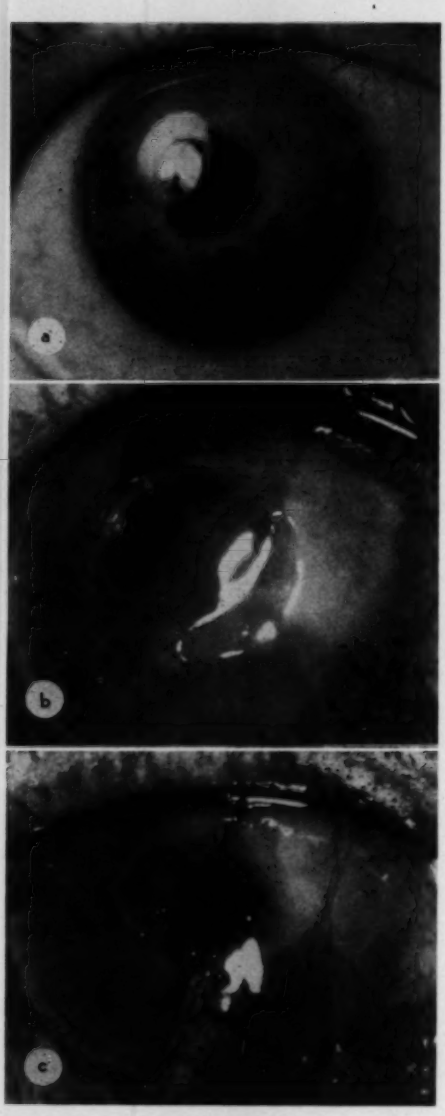


Fig. 12 (Leahey). J. F. (a) Clear corneal graft in 1953. History of recurrent dendritic and disciform keratitis in 1930, with reduction of vision to 1/200. Had removal of corneal vessels in 1949 by beta and a successful corneal graft in 1952, with 20/70 acuity. This patient also had incipient bilateral cataracts. Following uneventful cataract extraction in January, 1957, the graft was still clear.

(b) Chronic ulceration started eight years after beta radiation in the host cornea near the graft in an area originally subjected to 23,000 rep.

large deep vessels crossed the limbus nasally. Vision was 1/200 (fig. 12a).

In 1949, he received 15,000 rep on the 3-o'clock area. Six months later, he received beta on the 12-o'clock and 6-o'clock areas, and also two more treatments on the 3-o'clock area for a total of 21,000 rep at 3-o'clock. Because of overlapping treatment, he probably received 10 percent more between the 3- and 4-o'clock positions for a total of 23,000 rep.

Convalescence was uneventful with very little irritation at any time. In 1952 he had a corneal transplant which healed well and remained clear. Because of an immature nuclear cataract (not radiation type) vision was 20/70. This was his better eye as the left eye had amblyopia ex anopsia and an incipient cataract.

The cataracts gradually became worse and an intracapsular cataract extraction was done five years after the graft on January 7, 1957. The graft was slightly less clear following lens extraction but vision again was 20/70.

About June 1, 1957, the patient noticed slight redness and irritation of the eye. When first examined 17 days later he had a small ulcer at the 3:30-o'clock position in the old host cornea close to the graft. The graft showed moderate edema (fig. 12b).

The ulcer gradually spread to a diameter of about three mm. with secondary infection involving the graft. There was a sharply defined necrotic slough at the bottom. In about two months, the necrotic slough disappeared leaving a circumscribed pit with semiclear border and bottom. On October 11th, it perforated and a small bead of vitreous plugged the wound. A conjunctival flap was applied but it retracted in two weeks, again uncovering the open hole (fig. 12c). A second flap has remained in place. The eye remained intensely inflamed for three months but it was a whole year before this eye was completely free of inflammation. A regraft has not yet been done but, since the overradiated area was small, the eye appears suitable for a new transplant.

CASE 2

M. B. This man (aged 50 years in 1949) was pushed into a lime vat 40 years earlier and had complete vascularized leukomas of each cornea with vision of light projection only. Ten and eight years earlier, two attempts were made to strip off the thick pannus from the right cornea but each time scar tissue had grown over more profusely. No radiation had been given (fig. 13a).

In May, 1949, a superficial keratectomy was done with a recession of the conjunctiva and scar tissue around the limbus, followed by seven beta treatments given at four different areas for a total of 15,000 rep to each of four areas. Because of overlapping some areas may have had 20,000 rep.

←(c) The ulcer finally perforated and was covered by a conjunctival flap. The first flap retracted, exposing the fistula as shown here. A second flap held well and is still in place (one year later) and the eye is free from irritation. This eye appears suitable for a new graft.

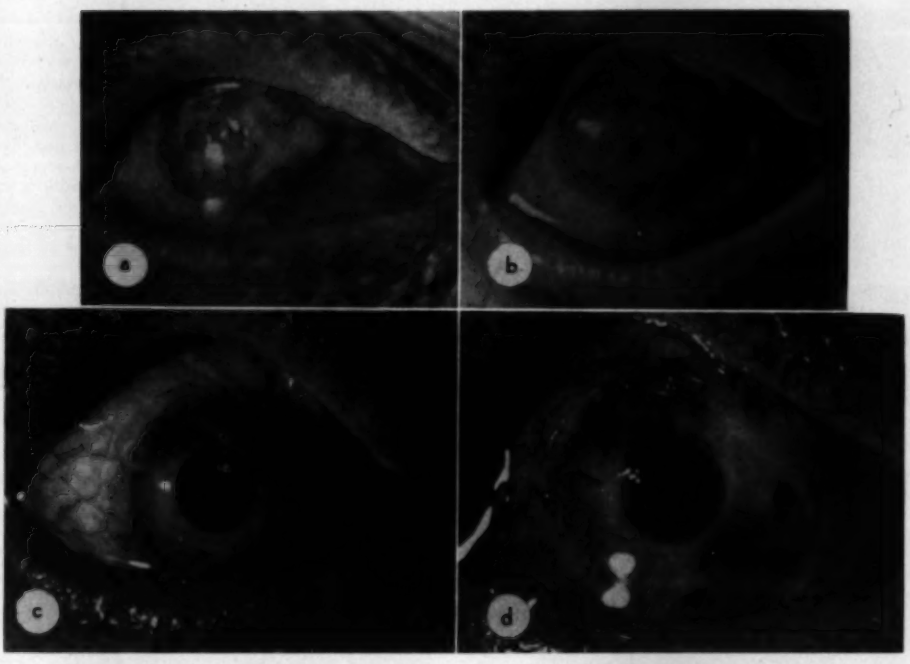


Fig. 13 (Leahey). M. B. (a) Complete thick pannus from lime burn 40 years earlier. (b) Same cornea after superficial keratectomy, resection of scar tissue and conjunctiva beyond limbus, and beta radiation. The cornea is now ready for a graft. (c) Clear graft four years after transplant and five years after beta. (d) Nearly healed corneal ulcer which occurred seven years after beta in an area of dense fatty degeneration, originally subjected to 20,000 rep. The nearly healed, sharply defined crater still shows near the 3:30-o'clock area. This cornea again showed superficial ulceration nine years after the beta.

The eye healed normally with no unusual prolonged inflammation and appeared free of vessels (fig. 13b).

A perforating graft was done in January, 1951, 20 months after beta. Despite the fact that it was set into dense opaque tissue over much of the circumference, the graft remained crystal clear and vision was 20/70 (fig. 13c). In May, 1956, five years after the graft and seven years after beta, he showed a slight irritation of the eye, more marked in the ciliary area nasally and also faint edema of the graft with reduction of vision to 20/200. Two weeks later, there was 3.0 by 4.0 mm. area of slight epithelial staining in a particularly dense area of scarring nasally. This portion of the leukoma had always consisted of yellowish white fatty degeneration with no evidence of any normal corneal tissue. This lesion developed into a very superficial ulceration with marked redness and persisted for three months (fig. 13d). After this, the peripheral part of the superficial ulceration healed but the central part formed a deep crater. At the end of five months, the slough at the bottom separated leaving the typical sharply defined pit with no slough on the edges or bottom. The base of the pit was almost down to Descemet's membrane.

This pit remained with little change for six months but gradually healed with avascular semitranslucent tissue to about 60 percent of the corneal thickness The total duration of the ulcer was 16 months. The corneal graft has continued to show variable faint epithelial edema with vision varying between 20/200 and 10/200. In January, 1959, 10 years after beta, there was again loss of superficial corneal tissue over the same 3.0 by 4.0 mm. area as the 1956 superficial ulceration. This healed in a month.

Case 3

Dr. J. G. This 39-year-old physician was seen in 1954. His left eye had been severely burned by sulfuric acid in 1934, leaving a completely vascularized leukoma with vision reduced to light projection (fig. 14a). Extreme divergent strabismus had developed subsequently. In August, 1954, a complete superficial keratectomy was done with recession of scar tissue and conjunctiva for four mm. beyond the limbus (fig. 14b). Over the next six weeks, nine radium D-beta treatments were given with two or three areas being treated each time.

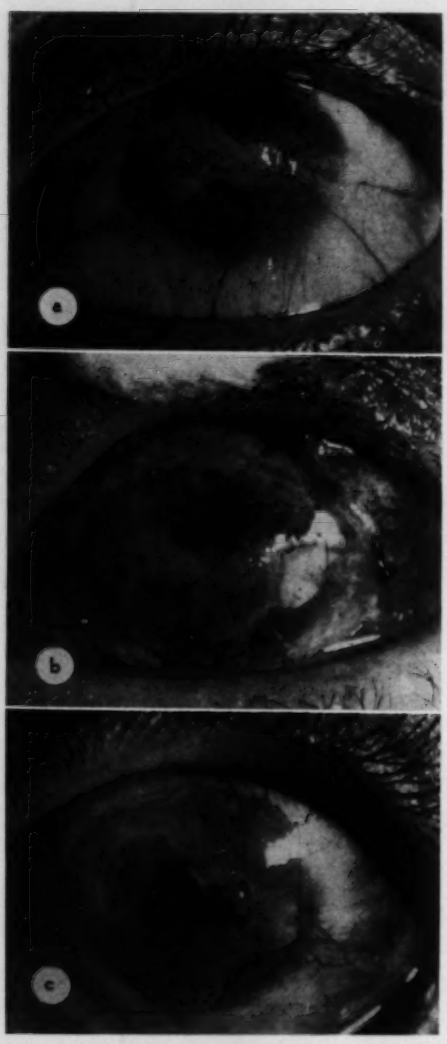


Fig. 14 (Leahey). J. G. (a) Vascularized leukoma in 1954 from a 1934 sulfuric acid burn. (b) Four days after superficial keratectomy, recession of conjunctiva and scar tissue. Beta was started on this day. (c) Same cornea 14 months after beta. It is nearly avascular and is now semitransparent. Three years after beta, an extremely superficial ulcer, 3.0 by 6.0 mm. developed centrally. This healed in five months without new vascularization or subsequent irritation.

The total amount to the entire eye was 72,000 rep. No more than five treatments were given on any one area, however, for a total effect of 18,000 rep; though due to overlapping, there may have been 22,000 rep on certain small areas.

A month after the last treatment, there was only faint irritation of the eye but many fine vessels persisted in the deep cornea. Two months later, the vessels had markedly decreased, the cornea was becoming more translucent and all irritation had disappeared (fig. 14c). From three months to eight months after cessation of the beta, there was again intermittent faint irritation of the eye and slight punctate areas of epithelial staining. Fourteen months after beta, the eye had been free of all irritation for six months. The cornea was almost completely avascular and was very much more transparent than formerly. The pupil could be easily seen and vision had improved from light projection to 6/200.

He was examined only once in 1956 at which time the eye was free from irritation. The patient stated, however, that it had been irritated occasionally for short periods during the year. Corneal sensitivity was markedly decreased.

Since vision in the other eye was 20/20, it was decided not to do a transplant but merely to straighten the eye. In January, 1957, a recession of the external rectus and a resection of the internal rectus was done with an excellent cosmetic result.

In June, 1957, there was superficial staining in the cornea over a central horizontal area 3.0 by 6.0 mm. This superficial ulcer persisted for five months but finally healed completely with no subsequent recurrence of sensitivity or ulceration. This ulcer was presumably a late complication of the radiation three years earlier.

CASE 4

M. G. Ulceration four years after beta. A summary of this case is given under the section on "Effect of beta on healing."

CASE 5

G. E. This 16-year-old boy was first seen in 1951. He had a complete heavily vascularized pannus from a chemical burn at age six, with light projection only (fig. 15a). In May, 1951, he had a superficial keratectomy with recession of conjunctiva and scar tissue for three mm. around the limbus. Over the next five weeks, he received 70,000 rep radium D-beta with a maximum of 18,000 in any single area. One month after stopping beta, he showed slight ciliary injection but the blood vessels were practically gone. Six months later, the cornea was avascular except in the periphery (fig. 15b). There was almost imperceptible ciliary injection but the eye was rather light sensitive. A year and a half later, there was still faint ciliary injection and the corneal vessels had grown back two mm. from the limbus.

The following year, the eye was free from inflammation most of the time, but at intervals showed punctate epithelial staining. In late 1954, three and a half years after beta, he showed a chronic superficial ulceration 2.0 by 4.0 mm. wide in the lower third of the cornea which he later reported lasted for six months.

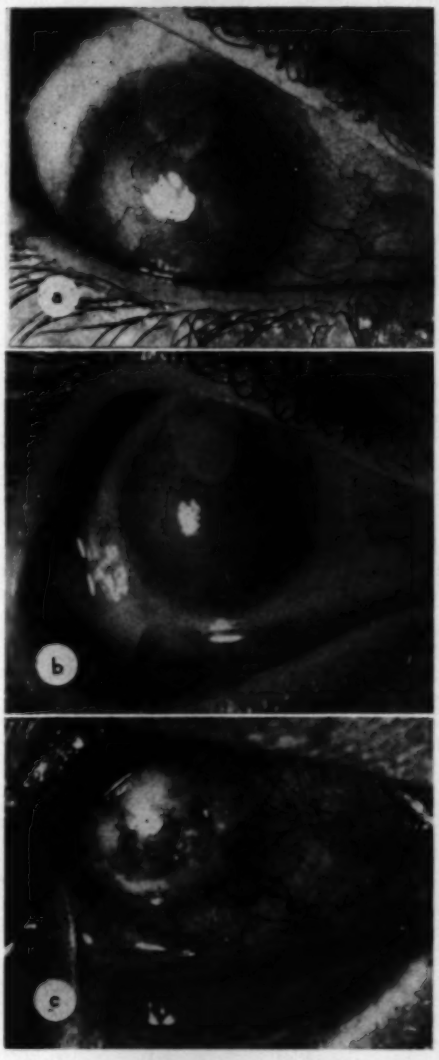


Fig. 15 (Leahey). G. E. (a) Dense panus from 1941 chemical burn.

(b) 1953. Same eye one year after superficial keratectomy, recession of conjunctiva and scar tissue around limbus and beta radiation. Ninety percent of the vessels had disappeared but the eye still showed intermittent slight irritation so the corneal graft was postponed.

(c) Seven years after beta. During the first three years, there were several episodes of mild irritation lasting two to four weeks, but no ulceration. At the end of three and one-half years, a superficial radiation ulcer, 2.0 by 3.0 mm. appeared on the lower central cornea. This healed in five months but recurred at intervals. Seven years after beta this eye still showed periodic irritation and the cornea contained areas of lipoid degeneration and new vascularization. The eye is unsuitable for corneal transplantation.

⟹

He was not seen again by me, however, for two years. At this time, (June, 1957) he still complained of periods of irritation lasting several weeks with no symptoms for several months between bouts of inflammation. Tension was normal and vision was still good light projection. Scarring and vascularization had increased tremendously (fig. 15c). Since the eye would obviously never be suitable for a graft and since vision was 20/20 in the other eye, it was felt than an enucleation should be considered and an artificial eye would give a better cosmetic effect.

In this case the ulcer was active for six months starting three and a half years after beta. Since this eye had intermittent irritation at intervals during the three and a half years before ulceration, it falls into an intermediate category slightly different from the group in which late ulceration occurred without the slightest evidence of inflammation in the long intervening period.

CASE 6

F. D. On November 4, 1949, a very large pterygium was removed from the right cornea by McReynolds transplant in the Massachusetts Eye and Ear Infirmary Clinic. A large rapidly growing recurrence was excised on January 3, 1950, and five radium D-beta treatments were given at one-week intervals for a total effect of 30,000 rep over the involved area. This was divided into 15,000 rep in each of two areas as the pterygium was very large, but due to overlapping the center of the area, received the full 30,000 rep. Despite the combination of pterygium removal and heavy beta radiation, there was only moderate irritation for three or four weeks and an apparently uneventful recovery. The eye was completely well for six and one-half years.

On July 17, 1956, the patient complained the eye had been sore, red, and tearing for two weeks. Examination showed slight infiltration and some loss of superficial tissue over the heavily radiated area (fig. 16). On August 3rd, he still showed faint staining but on August 10th, there was no further staining and the eye was almost free of irritation.

When next seen on February 1, 1957, he showed a shallow 3.0 by 4.0 mm. ulcer near the head of the pterygium of about one week's duration. By February 8th, this staining area had healed completely.

I did not see this patient myself in 1956 or 1957 and I am not sure how closely the keratitis resembled the indolent radiation ulcer found in the

Fig. 16 (Leahey). F. D. (1956). Ulcer six and one-half years after apparently successful radiation (January, 1950) for a large recurrent pterygium. A total of 15,000 rep was given in each of two areas but due to overlapping the central area was overtreated, receiving 30,000 rep. There had been no inflammation or irritation during the entire six and one-half years intervening. This ulcer healed in two weeks.

other cases. The history, location, and photograph of the ulcer, however, suggest that this recurrent break-down of tissue was a direct late complication occurring six and one-half and seven years after apparently successful beta radiation therapy. This was the only radiation ulcer which healed rapidly, probably because this was the only cornea which was in relatively normal condition.

Discussion

The six cases with this very late ulceration represent only 1.8 percent of the approximately 320 eyes we have treated with beta since 1948. The five with prolonged ulcers had certain common factors. Each of them originally had an extensive heavily vascularized leukoma of the cornea. In four of them, the leukoma was practically complete, and in the fifth the lesion involved 80 percent of the cornea. All had numerous deep vessels so that more radiation was required than in the average case. The four cases with the most severe scarring were all chemical burns. Each of the four most severe cases had a preliminary superficial keratectomy with recession of conjunctiva and scar tissue around the limbus just before starting beta.

In order to treat the deeper vessels adequately, approximately 25 percent more beta than usual was given each area. In most of these cases, the entire cornea and four mm. of area around the cornea had to be radiated. Different series of treatments were given to different areas so, undoubtedly, there was some overlapping. The average dosage to any one area on the cornea was about 18,000 rep but it is probable that on some overlapping areas the total dosage was approximately 22,000 rep. In the sixth case (the recurrent pterygium) the area of ulceration had received 30,000 rep due to overlapping.

This late necrosis of the cornea is not at all surprising. Similar tissue breakdowns many years after radiation have frequently been found in most other tissues of the body. They have been especially common in the skin presumably because they have been easy to recognize.

Greeley[23] mentions 50 years as the maximum period he found between radiation and development of ulceration or carcinomatous degeneration. Traenkle[24] found 55 cases of late radiation necrosis in 1,935 patients treated for skin cancer with over 50 percent of the lesions appearing more than two years after completion of therapy. Clinically, skin necrosis began with erythema and tenderness which increased at varying speeds. After separation of the slough, the ulceration usually has a clean sharply demarcated crater-like contour. Other authors speak of "a punched out ulcer with a sharp edge and necrotic base."

These descriptions of the skin ulcers are equally applicable to the corneal ulcers we have seen. Kritter and Vigneau[25] report 79 cases of bone degeneration and necrosis, the average time interval being 30 months after radiation.

Jones and Reese[22] describe two cases of necrosis of the sclera four and 14 years after radium treatment for conjunctival malignancy.

Merriam[21] reported two cases of scleral necrosis nine years and five and one-half years after radon therapy for conjunctival malignancy. Both of these cases also had cataracts coming on about five years after treatment. He also reports ulceration of the

cornea in a patient four and one-half years after successful, uneventful radon therapy for melanoma of the cornea near the limbus. This ulcer healed in 19 months but this boy also had a cataract. Twelve years after therapy the scar showed some calcification and was moderately vascularized. This case is apparently very similar to those in my series.

Since beta applicators have been widely used only since 1949 undoubtedly many more corneal ulcerations occurring three to eight years after successful radiation will soon be reported. It is reasonable to expect that during the next 10 to 40 years occasional malignancy of the cornea, conjunctiva, or sclera may also be found.

Effects of beta radiation on healing

The final important complication of beta radiation to be considered is the adverse effect on the healing of tissue.

In 1933, Ritchie[26] reviewed the literature and concluded that radiation retarded wound healing by causing "sluggishness of fibroblastic growth and an abnormality of the fibroblast."

Lushbaugh and Storer[27] in 1953 found that "while normal cellular exudates developed promptly, fibroblasts failed to appear in the periphery in irradiated areas." If the surgical incision was made before the area was irradiated, the fibroblasts that began to proliferate were arrested and underwent changes that resulted in the formation of giant abnormal forms.

In 1955, McDonald and Wilder[28] reported that beta radiation in doses commonly used clinically delayed healing of the corneal stroma in rabbits following incision through the central cornea or limbus. This interference with wound healing seems to be dependent primarily on the inhibition of fibroblastic proliferation. Radiation given as long as three months prior to surgery shows this effect to a similar degree as when given immediately before surgery. Hughes,[29] McDonald and Wilder, Castroviejo[30] and Leahey[6] have all reported cases of poor union of grafts following considerable beta radiation.

In my series, two cases showed definitely delayed union of the graft. In one eye (B. C.), with complete vascularized leukoma of the cornea (fig. 17a), the original graft done six months after partial superficial keratectomy and 15,000 rep of beta, healed

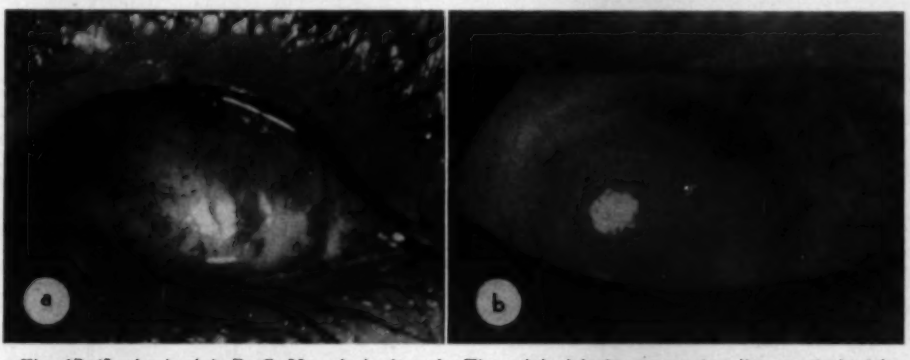


Fig. 17 (Leahey). (a) B. C. Vascularized graft. The original leukoma was heavily vascularized but improved with beta radiation. The first graft became vascularized and opaque and is shown here after more radiation. Note the small telangiectases. Four years after the original beta, this cornea also developed a small chronic ulcer which healed in four months. Five years after the original beta, a new corneal graft was done. There was delayed union of the entire lower half of this second graft.

(b) M. G. Dense leukoma from alkali burn following two partial superficial keratectomies and a total of 30,000 rep of beta radiation to each of three areas. A five-mm. perforating graft was done later, 14 months after beta. Despite perfect apposition, the lower half of the graft circumference had not healed by the 14th day but the incision did close during the next week.

satisfactorily but became opaque and vascularized. An additional 7,000 rep was given a year after the original beta (or six months after grafting). Four years after the original beta radiation, there was a small chronic ulcer of the cornea like the ones just described, presumably a result of the original beta radiation, although I did not suspect this at that time. Five years after the original beta radiation, a new corneal graft was done. There was delayed union of the entire lower half of the round graft and a low-grade chronic inflammation of the eye for another year. When the irritation finally subsided the cornea and the graft were again heavily vascularized. Fortunately glaucoma did not develop and visual acuity was still good light projection.

The second case (M. G.) (fig. 17b) received a severe alkali burn of each eye in May, 1951. The right eye had a dense white leukoma of the entire cornea with vision light projection only. In August, 1953, a partial superficial keratectomy was done and 16,000 rep of radium D beta was given to each of three areas. Since too much vascularization remained to allow transplantation, a more extensive keratectomy was done in February, 1954, and 14,500 rep were given to each of the same areas and also to one new site. The eye quieted down quickly and showed no irritation two months later. Most of the vessels disappeared.

In October, 1954, a five mm. penetrating graft was inserted with overlying plus two direct sutures. Despite perfect apposition the lower half of the graft circumference had not healed on the 14th day. The wound did close satisfactorily, however, during the next week leaving a good chamber; but there was eventual clouding of the graft and mild glaucoma. Despite the treatment with 30,000 rep there has been no later ulceration, but it is probable that this overtreatment was the cause of the delayed connective tissue response and slow healing.

Merriam[21] also described a patient who had a superficial keratectomy followed by 650 r of X rays (factors unknown) and later an additional 22,000 rep with a radon applicator. An eight mm. keratoplasty healed well but become cloudy so a total keratoplasty was done with a complete iridectomy and lens extraction. There was nonunion of part of the graft six weeks later and eventual enucleation. Merriam writes "the poor healing was felt by Dr. Castroviejo to be due to excessive radiation, and similar cases of his have confirmed this opinion."

Although radiation was given to a large number of other transplants, and although it is possible that all might show retarded proliferation of fibroblasts if examined under a microscope there was no gross clinical evidence of retarded wound healing in any other patients in my series.

Summary

Important features of beta radiation have been outlined with the observations being based partly on the literature and partly on our series of 320 human eyes treated with radium D beta since 1948. More recently we have also followed a few eyes treated with strontium 90.

Some of these observations are as follows:

1. Radiation is always destructive to tissue—never stimulating.

2. The effect of radiation is far greater on young tissue and growing cells.

3. When applied over the limbus, the beta from radon, radium, strontium 90 applicators has enough penetration to be cataractogenic. The radium D-E beta penetration is so limited that it cannot cause cataracts with ordinary clinical dosage and consequently appears to be the method of choice for removing superficial blood vessels on corneas, especially around the limbus.

For vessels in the posterior 25 percent of the cornea, the radium D applicator is moderately effective but definitely inferior to the other applicators; but because of the safety factor it still appears to be the treatment of choice in most cases. If the lens is already cataractous or absent, however, or if only the

central cornea is to be treated for this very deep vascularization, one of the other applicators is much more suitable as the superficial stroma would thus be subjected to less radiation and there would be less danger of late ulceration.

For palpebral vernal catarrh strontium 90 beta is more effective because of its greater penetration and is equally safe.

4. For a well-rounded program of safe and efficient therapy an ophthalmic radiation clinic should have at its disposal both the radium D and the strontium 90 applicators. There are also certain cases, including most malignancies, for which X-ray beta is more suitable (fig. 18) mainly because the entire area can be radiated without resort to the dangerous overlapping of treatment areas.

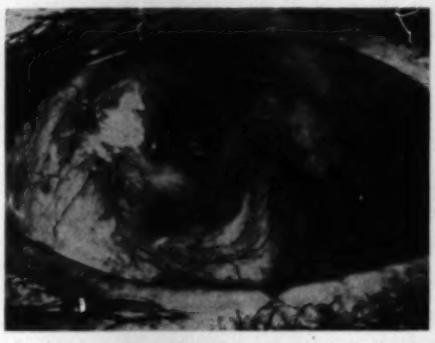


Fig. 18 (Leahey). Epidermoid carcinoma involving corneal and bulbar conjunctiva. Low-voltage X-ray therapy is indicated here rather than any type of applicator. By X rays the entire area can be radiated without resort to the dangerous overlapping of treatment areas. Since overlapped areas may receive double dosage, they may ulcerate years later.

5. In our series, we found that radium D-beta was extremely effective in treating: (a) corneal blood vessels preparatory to grafting; (b) rosacea keratitis; (c) recurrent pterygia; and (d) vernal conjunctivitis.

It is not indicated for most cases of interstitial keratitis and is contraindicated for dendritic keratitis, disciform keratitis, pyogenic ulcers, and malignancies around the lids.

6. The recommended dosage of radium D beta for removal of corneal vessels in the anterior 75 percent of the cornea is 3,000 rep given weekly five times for a total of 15,000 rep. For fine superficial vessels 11,000 rep is enough. If the vessels are in the posterior 25 percent of the cornea 18,000 to 20,000 rep are needed. For palpebral vernal catarrah four treatments of 1,500 rep for a total of 6,000 rep per treated area are sufficient.

It must be remembered that radium D applicators used in 1948 and several following years were calibrated in an entirely different and much less accurate manner than at present. Their output in rep measured by the currently standard extrapolation chamber method is four times greater than the rep output originally assigned these applicators (750 rep in early reports is the same as 3,000 rep in recent literature). This has caused great confusion about dosage and some acrimonious debate.

7. The main complications of beta therapy in the eye are as follows:

a. Cataract formation, with the damage beginning in the cells at the equator and typical radiation opacities showing in the posterior capsular region about two years later.

b. Ulceration of the cornea starting one to five months later, lasting for many months.

c. Detrimental effect on corneal healing for many years after radiation.

d. Ulceration of apparently normal corneal scar tissue many years later. This extremely late complication has been stressed for the first time. One to eight years after apparently successful uncomplicated beta ray therapy, corneal tissue which has been free from inflammation during intervening years suddenly breaks down into an indolent, chronic, sharply demarked radiation necrosis. This may heal in three to six months with additional scarring and vascularization, or it may perforate. If it heals it may again break down a few years later.

Ulceration of both early and very late types has occurred in occasional corneas after only 18,000 rep. This is more apt to occur if the cornea is in opaque degenerated condition before beta. Ulceration has not been

found in any eye with a semihealthy cornea except in one exposed to 30,000 rep. Ulceration has been much more common in heavily vascularized leukomatous corneas which were also subjected to superficial keratectomies. Since all of the most desperate pannus cases had this keratectomy before beta, it is impossible to prove from this series whether or not the preliminary keratectomy actually increased the tendency to ulcerate. It is probable however, that this is a negligible factor.

In summary, it should be borne in mind that beta radiation is a two-edged sword and its use entails possibility of very grave damage to ocular tissue. The zealous overtreatment of earlier years should not be repeated and radiation should not be used on any eye where a similar effect can be obtained by any other mode of treatment.

Despite the complications outlined in this paper, we must remember that nearly all of these eyes with complications were eyes that were originally blind, densely scarred, and heavily vascularized. Since they were hopeless without treatment, relatively little harm was actually done.

In general, the results of the 320 case series were remarkably good. Beta radiation, when administered properly, is a very valuable adjunct to ophthalmic treatment and constitutes one of the greatest advances in ocular therapy in recent years.

9 Central Street.

References

1. Iliff, C. E.: Beta ray radium applicator for ocular use, preliminary report. Arch. Ophth., **38**:827, 1947.
2. Burnham, C. F., and Neill, W., Jr.: Use of beta ray of radium applicator: Description of method and result obtained in superficial lesions of the eye. South. M. J., **33**:279, 1940.
3. Evans, R. D.: Radioactivity units and standards. Nucleonics, Oct., 1947.
4. Wolfson, H.: Canadian Radium and Uranium Corp. Personal communication.
5. Stevenson, W.: Ophthalmic applicator for beta radium-D. Mississippi Valley M. J., **70**:242, 1948.
6. Leahey, B. D.: Penetrating keratoplasty. Tr. Am. Ophth. Soc., **55**:575-636, 1957.
7. Friedel, H. L., Thomas, C. I., and Krohmer, J. S.: Description of sr. 90 beta-ray applicator and its use on the eye. Am. J. Roent. & Rad. Therapy, **65**:232, 1951.
8. Krohmer, J. S.: Physical measurements on various beta-ray applicators. Am. J. Roent. & Rad. Therapy, **66**:79, 1951.
9. Okrainetz, C. L.: Radiotherapy of diseases of the eye. Arch. Ophth., **48**:525, 1952.
10. Wilson, F. M., and Wilson, J. W.: Radioactive strontium therapy of the eye. Arch. Ophth., **48**:686, 1952.
11. Iliff, C. E.: Personal communication, 1953.
12. Hughes, W. F., Jr.: Beta radiation with strontium applicator. New England Ophth. Soc., April, 1953.
13. Lombardo, M.: Recession of limbal conjunctiva. Am. J. Ophth., **30**:1109-1113, 1947.
14. Milner, J. G.: Irradiation cataract. Brit. J. Ophth., **18**:497-511, 1934.
15. Friedenwald, J., et al.: Ophthalmic Pathology. Philadelphia, Saunders, 1952, p. 276.
16. Cogan, D. G.: Chemical and pathological characteristics of radiation cataract. Arch. Ophth., **47**: 55-70, 1952.
17. Leinfelder, P. J.: Discussion of "Lens surgery in radiation cataract." (Putenney, I., and Shoch, D.) Tr. Am. Ophth. Soc., **51**:299, 1953.
18. von Sallmann, L.: Experimental studies on early lens changes after roentgen irradiation. Arch. Ophth., **47**:305, 1952.
19. Shoch, D., and Putenney, I.: Ionizing radiation cataracts. Quart. Bull. Northwestern Univ. M. Sch., **28**:359-363, 1954.
20. McDonald, J. E., Hughes, W. F., and Peiffer, V. G.: Beta radiation cataracts. Arch. Ophth., **53**: 248-259, 1955.
21. Merriam, G. R., Jr.: Late effects of beta radiation on eye. Arch. Ophth., **53**:708-717, 1955.
22. Jones, I. S., and Reese, A. B.: Focal scleral necrosis. Arch. Ophth., **49**:633-636, 1953.
23. Greeley, P. W.: Am. J. Surg., **83**:342, 1952.
24. Traenkle, H. L.: Arch. Derm., **72**:446-453, 1955.
25. Kritter, H., and Vigneau, J.: (J. Radiol. et Electrol., **36**:786-789, 1955.) Quoted from Year-Book of Radiology. Chicago, Year-Book, 1956-57, p. 403.
26. Ritchie, G.: Effect of roentgen irradiation on the healing of wounds. Arch. Path., **16**:839-851, 1933.

27. Lushbaugh, C. C., Storer, J. B., and Hale, D. B.: Experimental acute radio-dermatitis following beta radiation. Cancer, **6**:671-682, 1953.
28. McDonald, J. E., and Wilder, H. C.: Beta radiation and corneal healing. Am. J. Ophth., **40**:170-180 (Nov. Pt. II) 1955.
29. Hughes, W. C.: Discussion of reference 21.
30. Castroviejo, R.: Quoted in reference 21.

THE ANATOMY OF THE LOWER EYELID*

And its relation to the cause and cure of entropion

Lester T. Jones, M.D.
Portland, Oregon

This study was undertaken not only because entropion is so frequently seen in elderly people but also because there has been so much dissatisfaction with the multiplicity of methods devised to cure it. It is quite possible that our many failures are due to a faulty concept of the mechanism that produces this condition. For the purposes of this paper "senile spastic entropion" and "senile entropion" of the lower lid will be considered as essentially the same. "Cicatricial entropion" has an entirely different etiology and will not be included in this discussion.

Normal anatomy

The lower lid subtends an arc of varying degrees of curvature, depending on the pressure of the globe against it, being greater in youth and less in old age. From without inward it consists of the following layers:

1. *Skin and subcutaneous fascia.* This is a thin, somewhat elastic layer and over the tarsal region is fairly well fixed to the underlying muscle and contains no fat. Below the level of the tarsus it becomes more mobile and contains progressively more fat and fascia as the orbital rim is reached. It receives certain muscle fiber insertions to be described later.

2. *Muscle.* This is made up of the palpebral part of the orbicularis oculi muscle. Although in appearance it is one continuous muscle, it has been divided arbitrarily not only from the rest of the orbicularis (orbital part) but also into two important subdivisions within itself.[1] They are the pretarsal muscle, overlying the tarsus and the preseptal muscle, overlying the septum orbitale (fig. 1). This division is most important because of the difference in origin, insertion, and action of each part:

a. The lower pretarsal muscle arises in a superficial head from the anterior part of the medial palpebral ligament and a deep head (Horner's muscle) from the posterior lacrimal crest (fig. 2). These join at the medial end of the tarsus. The muscle is firmly attached to the entire length of the tarsus and, at the lateral commissure, joins the upper pretarsal muscle to form a common tendon which is about eight mm. long and inserts into the lateral orbital tubercule (fig. 3). This tendon is erroneously called, in my opinion, the "lateral palpebral ligament" (which is described as attaching to the lateral ends of the two tarsi).[2] Along its upper border this tendon has a firm connection with the lateral expansion of the tendon of the levator palpebral superioris muscle.

b. The lower preseptal muscle arises anteriorly from the anterior part of the medial palpebral ligament and posteriorly from the lacrimal fascia. As it passes laterally the main part forms a continuous layer with the lower pretarsal muscle above and the orbital part of the orbicularis muscle below. A definite superficial group of its fibers pass from the medial palpebral ligament laterally

* Presented at the annual meeting of the Pacific Coast Oto-Ophthalmological Society, May, 1959, Las Vegas, Nevada.

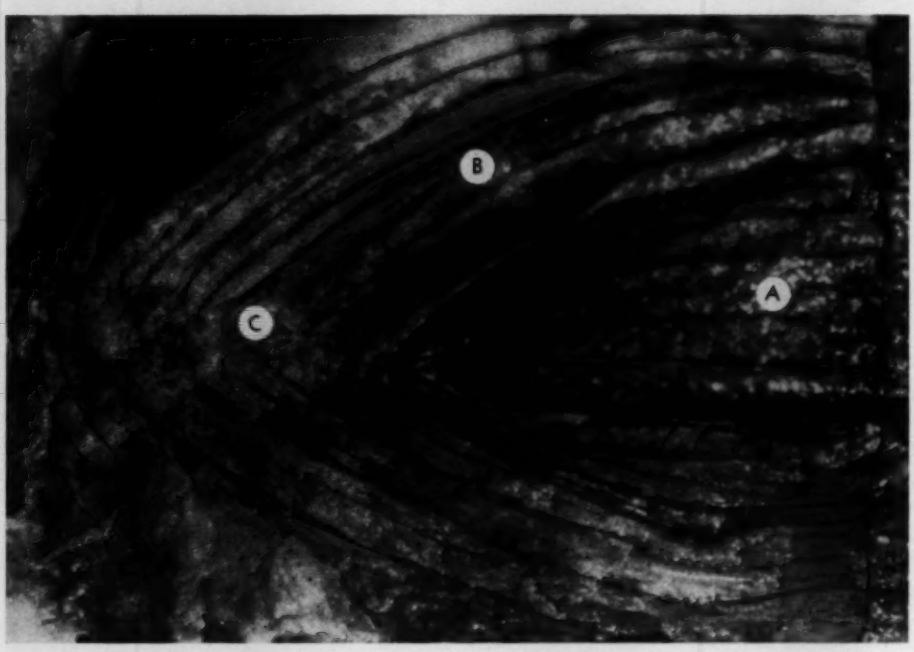


Fig. 1 (Jones). Lateral part of palpebral muscle. (A) Pretarsal muscle (upper). (B) Preseptal muscle (upper). (C) Lateral palpebral raphé.

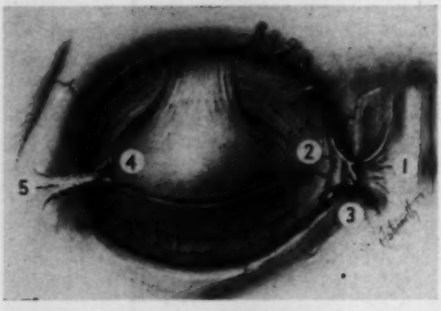


Fig. 2 (Jones). Attachments of palpebral muscle.

1. Anterior part of medial palpebral ligament. The superficial part of each preseptal muscle arises from its margins.
2. Posterior part of medial palpebral ligament. The deeper part of each preseptal muscle arises from it. The upper also arises from the posterior lacrimal crest.
3. Stump of ligament from which the superficial head of both pretarsal muscles arise.
4. Common tendon of insertion of each pretarsal muscle (called the lateral palpebral ligament).
5. Lateral palpebral raphe for insertion of preseptal muscle (a few fibers of the pretarsal muscle may also insert into it at times).

and slightly downward to insert fanlike, directly into the skin of the medial half of the lid (muscle of Merkel[3]).

The main body of the muscle is adherent to the septum orbitale although less firmly than the pretarsal is to the tarsus. Laterally the muscle bundles either form loops continuous with the upper preseptal bundles or interdigitate with them (fig. 4). In either case they are caught up in a dense, slightly elastic fascia to form the lateral palpebral raphe. Medially the raphe is attached to the pretarsal tendon at the lateral commissure and laterally to the dense fascia which invests the rest of the orbicularis muscle in the zygomatic region.

3. *Tarsal-fascial layer* (fig. 5). This layer may be divided into five parts: (a) the inferior tarsus and (b) its direct extension, the septum orbita'e which in turn is joined by (c) a layer of fascia from the sheath of the inferior oblique muscle. (d) The expansion of Tenon's fascia from the insertion of

Fig. 3 (Jones). Dissection showing common tendon of pretarsal muscles. (C) as it inserts into the lateral orbital tubercle of the malar bone.

the inferior rectus muscle joins the tarsus just posterior to the attachment of the septum orbitale. The inferior rectus fascia also acts as the origin and insertion of (e) the inferior palpebral muscle.[4]

4. *The palpebral conjunctiva.* This layer is almost inseparable from the posterior surface of the tarsus and inferior to the tarsus and is quite firmly attached to the fascial layer beneath it as far back as the lower fornix.

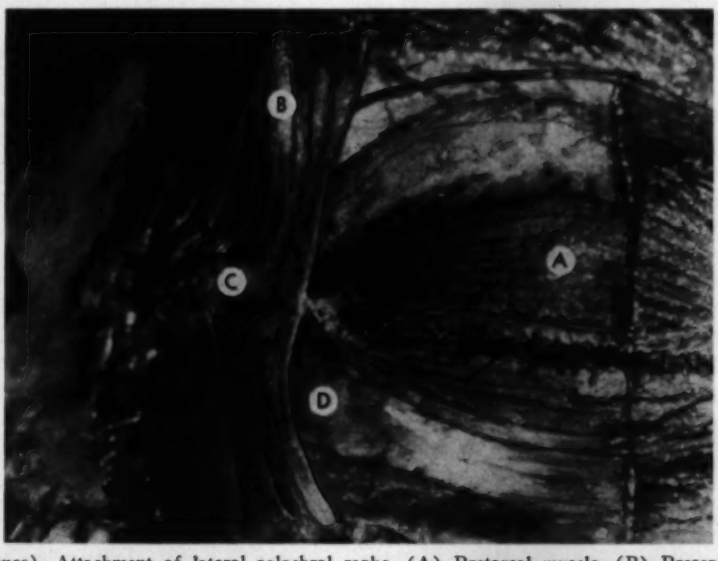


Fig. 4 (Jones). Attachment of lateral palpebral raphe. (A) Pretarsal muscle. (B) Preseptal muscle. (C and D) Attachment of medial end of lateral palpebral raphé to common tendon of (A).

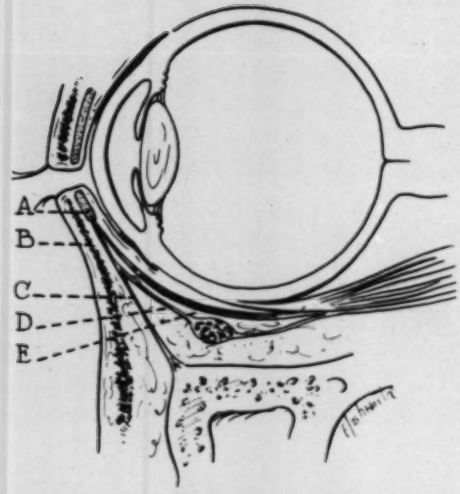


Fig. 5 (Jones). Schematic drawing showing cross-section of lower lid in young adult: (A) Tarsus. (B) Muscle. (C) Septum orbitale. (D) Fascia of inferior oblique muscle. (E) Fascial sheath from inferior rectus muscle with the inferior palpebral muscle.

Physiology

On inspection it can be seen that the lower lid is quite mobile. It can be stretched upward from 10 to 15 mm. depending on the prominence of the globe and the age of the person, stretching more as age progresses. From the position of direct gaze the lower lid margin is about level with the lower limbus. As the eye rotates upward from this position to its full extent, about 45 degrees or seven mm., the lower lid follows it roughly one third of this distance. This is due to the pull of the upper lid structures at the lateral canthus and the contraction of the lower preseptal muscle.

From the position of direct gaze the eye can be rotated downward about 55 degrees or 10 mm., the lower lid following roughly half of this distance due to the pull of the fascia from the inferior rectus muscle with some assistance from the inferior palpebral muscle and inferior oblique fascia.

The medial commissure is relatively fixed while the lateral commissure is somewhat mobile. It is prevented from any anterior, medial displacement by the rigid tendon of the pretarsal muscle but, because of the elasticity of the lateral palpebral raphe, it can move in other directions a few mm., depending on rotations of the globe and blinking.

The action of the palpebral part of the orbicularis oculi muscle is voluntary and involuntary; the action of the orbital part is voluntary. When the whole muscle contracts as in squeezing the eye shut, the surrounding skin and fascia is pulled toward the medial canthus (1) upward and medially from below, (2) medially from the side and (3) downward and medially from above, causing marked infolding of the skin over the eyelids with each tarsus exerting considerable pressure against its fellow and the elasticity of the lateral palpebral raphe and septum orbitale allowing the preseptal muscles to override the corresponding parts of the pretarsals nearly to their origins. The "squeezing" forces the globe deeper into the orbital fossa which in turn pulls the lower border of the lower tarsus backward, thus preventing a "physiologic" entropion whenever squeezing occurs.

Pathology

When senile entropion develops, certain changes have taken place in the anatomy and physiology of this area (fig. 6):

1. Some degree of enophthalmos, due to absorption of orbital fat has occurred, reducing the pressure of the globe against the tarsi.

2. The skin and superficial fascia have become atonic, redundant and less adherent to the underlying preseptal muscle.

3. The lower preseptal muscle has become less fixed to the underlying septum orbitale and begins to lose its pressure against the base of the tarsus, moving upward over the pretarsal during moderate contractions of the muscle.

4. The deep fascial layers attached to the base of the tarsus have become relaxed, not only by the enophthalmos but also by the

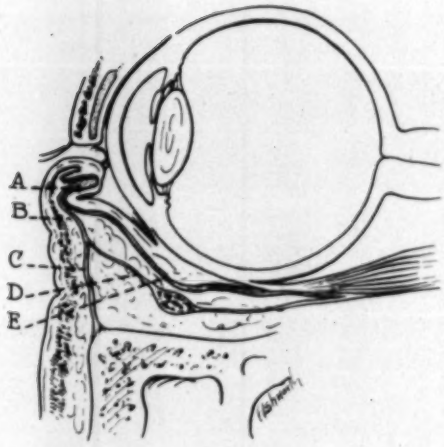


Fig. 6 (Jones). Same as Figure 5 in old age with relaxed fascia, enophthalmos, and entropion.

usual atony that accompanies the aging process.

All of these factors tend to decrease the pressure against the lower margin of the tarsus and increase it against the upper margin, allowing the tarsus to tumble from 90 to 180 degrees.

Surgery

It can be seen that entropion of the lower lid is somewhat analogous to ptosis of the upper lid in that the cure for each condition lies in shortening its retractors, that is, the depressors of the lower and the elevators of the upper.

To hold the lower margin of the lower tarsus down, it would appear that two procedures are necessary: (1) to shorten the deep fascias by resecting enough to restore an adequate downward and backward pull on the tarsus and (2) to reattach the preseptal muscle to this fascial layer beneath the tarsus in order to restore its elevating power and prevent it from overriding the tarsus above. A third procedure might also be considered and that is to fix the skin to this same deep fascia through a longitudinal slit between the pretarsal and preseptal muscles. This could be done either with or without resecting redundant skin and would create a connective tissue barrier, making it more difficult for the preseptal muscle to override the tarsus.

To fulfill these requirements the following techniques are offered:

1. *Conjunctival approach* (fig. 7). Local anesthesia by infiltration should be adequate in nearly every case. An Ehrhardt lid forceps is applied with the flat blade outward and the short one grasping the tarsus just inside of the lid margin. The lid is everted and two parallel incisions 12 to 14 mm. apart are made through the conjunctiva and fascia but not through the muscle. These should be in the medial third of the lid, starting at the lower border of the tarsus and extending towards the fornix for about 12 mm.

A tunnel is made by blunt dissection as near the inferior border of the tarsus as possible and one leg of a muscle clamp inserted. The conjunctiva-fascial layer is fixed by the clamp and cut free from the tarsus. The flap is then carefully dissected free from the preseptal muscle to the desired length. The exposed part of the preseptal muscle is separated from the pretarsal by blunt dissection.

The next step is to place a row of three double-armed, 4-0 mild chromic or silk mattress sutures through the flap from the conjunctival side, six mm. from its tarsal end and bring them out through the conjunctival side of the lower border of the tarsus. The excess tissue between the clamp and the sutures is excised and the sutures drawn up and tied. Two 4-0 black silk mattress sutures are inserted in the flap three mm. below the level of the first three in such a way that one straddles the lateral and the other the medial margin of the flap. These sutures are passed between the two separated muscles out through the skin about six mm. below the margin of the lid and each is tied over a rubber stint.

No bandage is necessary and the black silk sutures are removed on the fifth day.

2. *Cutaneous approach* (fig. 8). Anesthesia as already described. The lid is stretched upward and a horizontal incision, at least

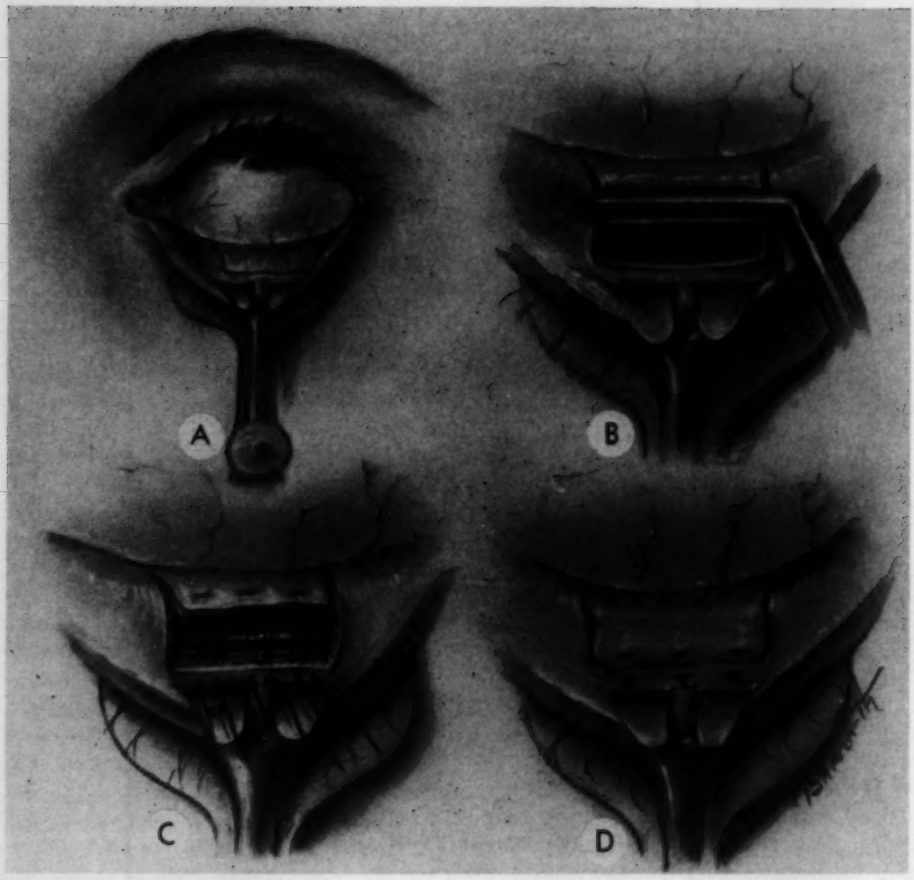


Fig. 7 (Jones). Surgery by conjunctival route: (A) Incisions. (B) Flap grasped by muscle clamp. (C) Sutures in place after resection of distal six mm. of flap. (D) Closure.

25 mm. long and about seven mm. from the lid margin, is made in the skin. The skin edges are dissected free and the muscle split horizontally at the base of the tarsus. The lower muscle (preseptal) is dissected free from its fascial base over an area of about 15 mm. Two parallel incisions, 12 to 14 mm. apart, are made through the fascial-conjunctival layer in the middle third of the lid. These should begin at the lower margin of the tarsus and extend downward and posteriorly about 12 mm. The flap is then cut free from the tarsus and three double-armed, 4-0 mild chromic gut sutures are placed through it about six mm. from its cut end. The end of the flap distal to the sutures is then resected and the sutures passed through the base of the tarsus and tied.

The last step is to try to make a connective tissue barrier between the skin and fascia which will prevent the preseptal muscle from overriding the tarsus. As the skin is usually quite redundant, a generous elipse should be resected from the lower margin of the incision and two mattress sutures passed from the conjunctival side, as already described, through the gap in the muscles, and tied over a stint beneath the lower skin margin. The

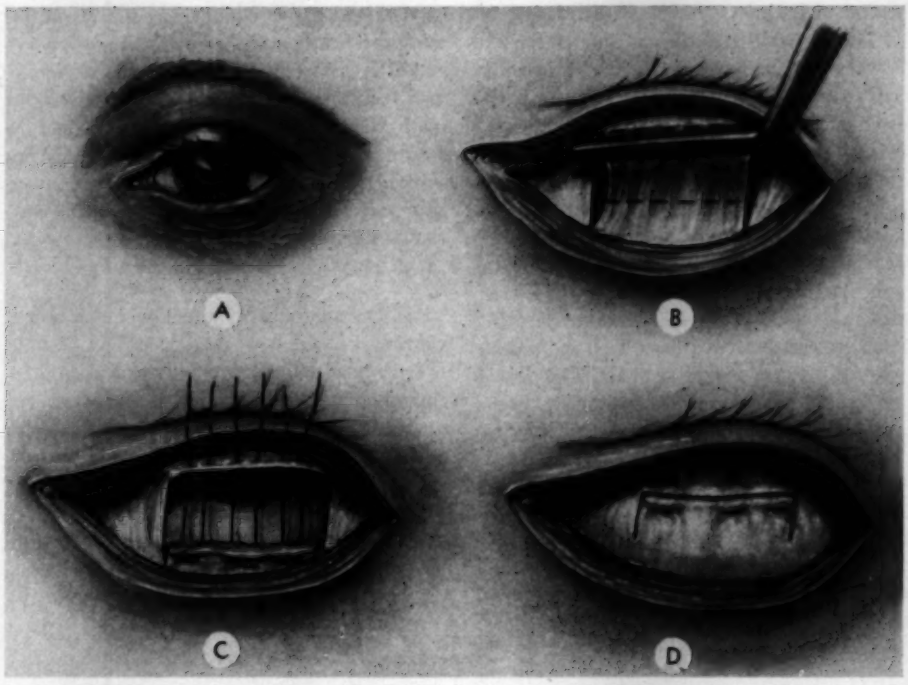


Fig. 8 (Jones). Surgery by cutaneous route. Steps essentially the same as in Figure 7. Not shown are the excision of skin nor final mattress suture between conjunctival-fascial layer and skin.

skin incision is closed with a running suture that takes a bite in the underlying fascia with each stitch.

It is possible that older surgical methods, if modified to take advantage of some of these anatomic requirements, may become more effective without shortening the tarsal-fascial layer. As examples the following six methods are cited:

1. *Excision of an elipse of skin* (Celsus[5]). The primary incision should be made just inferior to the lower margin of the tarsus, the preseptal muscle split from the pretarsal, the skin elipse removed and the skin edges sutured to the septum orbitale.

2. *Subcutaneous sutures* (Gaillard,[6] Snellen[7]). This consists of three mattress sutures which should enter the skin at the level of the lower border of the tarsus, passing through the muscle layer just below the tarsus and then entering the septum orbitale at a lower level, emerge in the infra-orbital region as described by the authors. The resulting connective tissue bands might then form a better barrier to the preseptal muscle.

3. *Ziegler cautery* (Ziegler[8]). The row of punctures should be just below the lower margin of the tarsus and deep enough to create scar tissue reaching through the muscle to the septum orbitale.

4. *Buried skin flaps* (Machek[9]). These should be brought down through tracks posterior to the preseptal muscle instead of subcutaneously in order to prevent the muscle from rising above the level of the horizontal skin incision.

5. *Wheeler's operation* (Wheeler[10]). Instead of the pretarsal muscle, a strip of the preseptal muscle, five or six mm. wide, should be cut and overlapped and then sutured to the septum orbitale.

6. *Butler's procedure* (Butler[11]). This

method of taking a V-shaped section out of the lower part of the tarsus should include the preseptal muscle layer in the sutures. In fact it might increase its effectiveness if the lower mattress suture in the tarsus extended through to the skin and was tied over a stint.

Reeh's modification of also removing a triangle of skin below the outer canthus should also include cutting the preseptal muscle near its insertion in the lateral palpebral raphe and transplanting it downward. If necessary some of the end of the muscle could be excised to shorten it and keep the muscle tight against the septum orbitale. This would prevent it from overriding the pretarsal at the lateral canthus.

Comment

It would appear that any method that involves making a horizontal incision completely through the lid in the tarsal region and then suturing the lower conjunctival-tarsal edge to the upper cutaneous edge would be more safely accomplished by making the horizontal incision through only the skin and muscle at the level of the *lower* border of the tarsus. Then the upper skin margin could be sutured to the septal-fascial layer. The lower skin edge then could be sutured to the upper skin surface, making the firmest possible barrier to the migration of the preseptal muscle.

Summary

1. The anatomy of the lower lid is reviewed.

2. A new method for the surgical cure of entropion is offered, based primarily on resection of a tongue of conjunctival-fascial tissue at the base of the inferior tarsus, and reattachment of the preseptal muscle to the septum orbitale.

3. The application of these findings to improve results in older methods is discussed.

624 Medical Arts Building.

References

1. Whitnall, S. E.: Anatomy of the Human Orbit and Accessory Organs of Vision. New York, Oxford, 1932, ed. 2, p. 152.
2. Wolff, E.: The Anatomy of the Eye and Orbit. Philadelphia, Blakiston, 1954, ed. 4, p. 163.
3. Ibid.
4. Ibid.
5. Celsus, A. C.: Cited by Arruga, H.: Ocular Surgery. New York, McGraw-Hill, 1952, pp. 88, 182.
6. Gaillard, F. L.: Bull. Soc. Med. Poitiers, 1844. Cited by Arruga,[5] pp. 90, 93.
7. Snellen, H.: Modifications a l'operation de l'entropion. Cong. Period. Internat. Ophth., **2**:236, 1863.
8. Ziegler, S. L.: Galvanocautery puncture in ectropion and entropion. J.A.M.A., **53**:183, 1909.
9. Machek: Cited by Lebensohn, James E.: The Machek operation applied to the lower lid for the relief of senile entropion. Am. J. Ophth., **30**:504-507 (Apr.) 1953.
10. Wheeler, J. M.: Spastic entropion correction by orbicularis transplantation. Tr. Am. Ophth. Soc., **36**:157, 1938; Am. J. Ophth., **22**:477, 1939.
11. Butler, J. B. V.: A simple operation for entropion. Arch. Ophth., **40**:665, 1948; A simple operation for correction of senile entropion. Eye dig., 1:3, 1955.

PRESENT STATUS OF EXPERIMENTAL ISO-ALLERGIES IN RELATION TO THE EYE*

Ted Suie, Ph.D.
Columbus, Ohio

In recent years, growing emphasis has been placed on auto-immunity as a possible explanation for the etiology of such clinical entities as glomerulonephritis, hemolytic anemia, allergic encephalitis, hepatitis, as well as certain types of ocular disease involving the lens, uvea, or optic nerves.

Auto-immunity may be defined as a condition whereby an individual demonstrates pathologic changes due to antibodies pro-

* From the Department of Ophthalmology, Ohio State University.

duced against his own cells or tissues, while in iso-immunity (or iso-allergy) the individual demonstrates these effects against cells or tissues of only certain members within his species. A well-known example of this is transfusion accidents which result from incompatibility of iso-antigens contained in the red blood cells.

Iso-antigens may in a greater sense be found not only in certain individuals of a species but also in individuals of other species and may include the so-called organ-specific antigens. These latter antigens are found in all members of a species and occur in other species. The antigenic specificity is not determined by the species from which the antigen is derived but rather by the antigenic mosaic of the organ itself. An example of an organ-specific antigen is protein of lens since antilens sera, for example, produced in rabbits, will react with lens regardless from which species of animals the lens protein is derived.

A review of literature which covers the area of iso- and auto-allergy has shown that there is an ever-increasing awareness that autosensitization may play a significant role in clinical entities which previously were inadequately explained.

As early as the beginning of this century Elschnig[1-3] proposed an iso-allergic theory for sympathetic ophthalmia. He attempted to explain this ocular manifestation by the following reasoning:

When uveal tissue is destroyed by some mechanism the absorption of this tissue causes the formation of organ-specific antibodies which in turn sensitizes the remaining uveal tissue of the same eye as well as that of the opposite eye. He was able to demonstrate specific antibodies in the sera of rabbits which were injected intraperitoneally with heterologous and homologous uveal tissue. He believed that the uveal pigment was the antigenic component.

As a direct outgrowth of Elschnig's findings, McPherson and Woods[4] prepared uveal pigment for skin-testing patients having clinical signs of sympathetic ophthalmia. They summarize their findings by stating, "The diagnostic and prognostic significance of the skin sensitivity test is limited. Positive tests are cause for alarm and increased vigilance. Doubtful and negative tests lend slight comfort and indicate in general a better prognosis. However, the margin of error in both positive and negative tests is so great that their interpretation should be made only in the consideration of the clinical course."

Woods[5] was able to produce bilateral eye reactions in dogs by first injecting uveal pigment into the vitreous of one eye and later injecting the same antigen intraperitoneally. Henton[6] noticed an increase in the opsonic index for beef uveal pigment in patients receiving therapy with this material.

In 1933, Lucic[7] reported a method for preparing "uveal tissue toxin." He found that (1) repeated intracutaneous injections of heterologous (bovine) uveal tissue combined with staphylotoxin produced simultaneous sensitization to heterologous (swine), homologous, and autogenous uveal pigment in six out of 22 rabbits used, (2) repeated injection of uveal tissue devoid of staphylotoxin produced no sensitization to uveal pigment, and (3) sensitizing injections with homologous "uveal tissue toxin" produced no sensitization to uveal pigment in any of the 11 rabbits used. Cellular reactions confirmed by histologic sections were used as the criteria of hypersensitivity.

Thyroglobulin, casein, fibrinogen and alpha globulin of crystalline lens have been shown to have iso-antigenic properties and they all lack species specificity. Their specificity is probably dependent on the chemical nature of the substance from which they are produced and these proteins appear to have serologic similarities of the animals from which they may be derived.

Uhlenhuth[8] was one of the first to demonstrate organ specificity. He found that lenses of different species contain identical antigenic components since antisera to beef lens protein react serologically not only with the

homologous antigen but also with lenses of mammals, birds, and amphibians. This particular specificity revealed that the reaction is limited not by the species but by the organ from which the antigen was derived. Thus, these organ-specific substances act, under proper conditions, as foreign proteins in the animal body.

Later, Hektoen[9] enlarged upon this work by demonstrating that precipitation tests with lenses of different species—beef, chicken, dog, guinea pig, monkey, rabbit, rat, sheep, and swine—constantly showed organ specificity when reacted with antisera for beef, horse, human cataractous, sheep, and swine lenses. Furthermore, he proved that normal lenses of mammals did not demonstrate species specificity. He also reported that aqueous and vitreous humors may contain substances which react with lens antiserum. However, beef cornea, retina, and uvea did not appear to contain antigens common with the lens. Rabbits did not develop precipitins to homologous lens protein unless they had been injected previously with beef lens protein. This latter experiment has been open to some criticism since this reaction could have been an anamnestic response.[10]

Eleven years later, Burky and his coworkers[11] found that alpha crystalline of lens was the true specific substance. Furthermore, beta and gamma crystallines as a complex were inert in homologous species.

These researchers also reported that a positive precipitation test occurred with the sera of rabbits injected with homologous alpha crystalline fraction of whole lens but no precipitins were demonstrated if homologous whole lens were injected. They explained this finding by stating, "Beta and gamma crystalline, when combined with alpha crystalline in whole lens extract, so color the antigenic mosaic that in homologous species the antigenic properties of alpha crystalline are inhibited."

This fact could explain the absence of antibodies of the immune or allergic type when lens protein escapes due to the rupture of the capsule in many of the surgical cases.

Burky[12] succeeded in producing experimental endophthalmia phacoanaphylactica in rabbits by injections of lens and staphylococcal toxin. These animals demonstrated cutaneous reactivity to staphylococcal toxin and lens substance and developed a clinical and histologic condition resembling human endophthalmia phacoanaphylactica. This condition appeared only if the lenses of such animals were pierced with a needle. This study not only confirmed the organ specificity of lenses but also demonstrated that a well recognized clinical entity could be produced in animals when the eye was damaged.

Following this demonstration of organ specificity, many investigations were undertaken to determine whether or not other clinical conditions with obscure etiology might be due to autosensitization. To mention but a few, Smadel[13] worked on nephritis, Cavelti[14–16] on glomerulonephritis and rheumatic fever, and Boorman, et. al.[17] on acquired hemolytic anemia. In each instance, these investigators have presented experimental evidence that auto-immune mechanisms may indeed play a role in these various clinical conditions.

In recent years investigators have demonstrated the iso-antigenicity of nervous tissue. Lewis[18] reported that alcoholic extract of brain was the iso-antigenic fraction of this organ. He felt that the difficulty of demonstrating spontaneous iso-antibodies for brain antigen under physiologic conditions may be due to the blood-brain barrier. Furthermore, it is conceivable that in destructive brain lesions by infectious organisms, the conditions necessary for iso-antigenicity would be present if the antigen could reach the circulation.

Schwentker and his coworkers[19] found that rabbits injected with emulsions of aqueous or alcoholic extract of homologous brain developed few or no antibodies which were able to fix complement. However, if the brain was modified by allowing it to stand at room temperature for five to 30 days or if

the emulsion of homologous brain was experimentally infected with vaccinia virus, then complement fixing antibodies were produced in rabbits.

These discoveries of the organ specificity of brain immediately gave impetus to further study of the mechanisms of postvaccinal, as well as postinfectious, encephalidites.

Freund and his group[20] demonstrated increased antibody production, as well as a lasting sensitization to tuberculin, by inoculating monkeys with heat-killed tubercle bacilli suspended in paraffin oil.

Several years later, Freund and McDermott[21] noted that the duration of intracutaneous sensitivity to horse serum in guinea pigs injected with horse serum combined with a lanolinlike substance and killed tubercle bacilli suspended in paraffin oil, was longer than the duration of sensitivity obtained with living tubercle bacilli and horse serum. Also, the adjuvant increased the production of precipitins. They stated that "killed tubercle bacilli probably play the same role as the living ones, though their role has not been elucidated. Paraffin oil enhances the cellular reactions caused by the tubercle bacilli and protects the bacteria from destruction and sustains sensitization and antibody formation. Aquaphor may have two effects. It may retard the possible separation of horse serum; thus delaying destruction and elimination."

Freund and his coworkers[22] produced posterior paralysis in guinea pigs by a single injection of guinea pig or rabbit brain with a water-in-oil emulsion containing killed or living acid-fast bacilli. On the basis of cutaneous systemic reactions these authors concluded that this meningo-encephalomyelitis was probably allergic in nature. Further investigations have shown that even autologous brain tissue was capable of producing these immunologic manifestations.

Kabat, et al.[23] found that large doses of cortisone prevented local granulomatous response at the site of injection of tubercle bacilli into monkeys and subsequent injection of brain adjuvant emulsion did not produce acute disseminated encephalomyelitis. These authors stated that "since granulomatous tissue is thought to be involved in the formation of antibody to the brain tissue at the local inoculation site, the cortisone, by modifying the granulomatous response would reduce the formation of antibody."

Additional evidence that Freund's adjuvant enhances sensitivity was offered by Landsteiner and Chase[35] who produced contact dermatitis type of sensitization in guinea pigs to picryl chloride by means of intraperitoneal injection of this compound and killed tubercle bacilli suspended in paraffin oil.

In 1953, Fog and Bardram[24] reported iridocyclitis occurring in pigs having experimentally produced allergic encephalomyelitis. This finding was recently confirmed by Bullington and Waksman.[25] They reported that rabbits which were injected with homologous and heterologous central nervous tissue including optic nerve combined with Freund's adjuvant developed optic neuritis and iridocyclitis. These ocular signs occurred in approximately three fourths of the animals and the onset was concurrent with the onset of the allergic encephalomyelitis. The ocular clinical findings were confirmed by histopathologic studies. Animals inoculated with peripheral nerve with adjuvants did not demonstrate intraocular lesions.

Suie and Taylor[26] also were able to demonstrate optic neuritis in five rabbits inoculated with homologous brain tissue combined with Freund's adjuvant. Histologically the affected optic nerves showed extensive demyelination. Unfortunately the eyes were not preserved for histologic studies to determine the presence of iridocyclitis.

Neither Suie and Dodd[67] nor Bullington and Waksman[24] were able to produce isoallergic uveitis in rabbits inoculated in the footpads with homologous uveal tissue combined with Freund's adjuvant. Collins,[28, 29] however, reported that guinea pigs which were inoculated intramuscularly and intraperitoneally with macerated guinea pig uvea

and the adjuvant developed choroidal lesions which simulated those found in naturally occurring sympathetic ophthalmia. Approximately half of the animals treated in this manner exhibited areas of choroidal infiltration consisting of lymphocytes, plasma and epithelioid cells in addition to Dalen-Fuchs type nodules. Control animals which were injected with the adjuvants without uveal tissue demonstrated no eye pathology. The choroidal reactions were enhanced by administration of cortisone. A similar histopathologic picture was obtained in monkeys which were given intramuscular injections of homologous uvea and adjuvants. Naquin[30] was not able to confirm these observations. However, he did note that guinea pigs inoculated with homologous lens tissue mixed with adjuvant developed a tuberculinlike hypersensitivity to the lens.

It has been reported that a very small percentage of animals inoculated with homologous uveal tissue and adjuvant develop experimental allergic encephalitis.[25,27] These findings along with the findings that iridocyclitis may be produced by nervous tissue would indicate an antigenic relationship between nervous tissue and uveal tissue. That such a relationship may exist has been further strengthened by Suie[31] who demonstrated by complement fixation tests a cross reaction between rabbit uveal antisera and rabbit brain antigen. The results of Kabat, Wolf and Bazer[28] indicate that myelin might be the antigenic fraction involved in iso-allergic encephalitis. Alvord[32] demonstrated that the active fraction was present in phosphotidlike extracts of brain tissue and of optic nerves which contain only white matter.

Jeris and Koprowski[33] were able to produce paralysis in two out of 10 guinea pigs by using cerebroside and sphingomyelin fractions of the brain. However, three of 10 animals which received the protein fraction, remaining after the extraction of the lipids, also developed neurologic signs.

The foregoing review has shown that production of various iso-allergic manifestations in the eyes of experimental animals is possible; however, the true significance of such auto-immune mechanisms in naturally occurring ocular disease is not fully understood. Cavelti[34] has offered several possible explanations for auto-immunologic disease in man: (1) Auto-allergy could result when foreign proteins from micro-organisms, toxins, and so forth, unite with a tissue hapten after breakdown of tissue protein-hapten complex, or, (2) auto-allergy could result when tissue is modified by chemical or physical factors and thereby acting as an antigen with immunologic properties similar to the normal tissue. Antibodies thus formed to the modified tissue could react with the normal tissue.

Department of Ophthalmology (10).

References

1. Elschnig, A.: Studien zur sympthischin Ophthalmie. Arch. f. Ophth., **75**:507, 1910.
2. ———: Studien zur sympthischin Ophthalmie. Arch. f. Ophth., **76**:459, 1910.
3. ———: Studien zur sympthischin Ophthalmie. Arch. f. Ophth., **78**:549, 1911.
4. McPherson, S. D., and Woods, A. C.: The significance of the intracutaneous test for hypersensitivity to uveal pigment. Am. J. Ophth., **31**:35, 1948.
5. Woods, A. C.: Immune reactions following injuries to the uveal tract. J.A.M.A., **77**:1317, 1921.
6. Henton, H. O.: Opsonic index for uveal pigment in treated patients. Arch. Ophth., **17**:113, 1937.
7. Lucic, H.: Uveal tissue sensitization in rabbits by synergistic action of staphylotoxin. Proc. Soc. Exper. Biol. & Med., **40**:273, 1939.
8. Uhlenhuth, P.: Festschrift. zum sechsigsten Geburtstage von R. Koch. Jena, 1903.
9. Hektoen, L.: The specific precipitin reaction of normal cataractous lenses. J. Infec. Dis., **31**:72, 1922.
10. Woods, A. C.: Allergy and Immunity in Ophthalmology. Baltimore, Johns Hopkins Press, 1933.
11. Burky, E. L., Woods, A. C., and Woodhall, M. B.: Organ specific properties and antigenic power in homologous species of alpha crystallin. Arch. Ophth. **9**:446, 1933.
12. Burky, E. L.: Experimental endophthalmitis phacoanaphylactica in rabbits. Arch. Ophth., **12**:536, 1934.

13. Smadel, J. E.: Experimental nephritis in rats induced by injection of anti-kidney serum. J. Exper. Med., **64**:6, 1936.
14. Cavelti, P. A., and Cavelti, E. S.: Studies on the pathogenesis of glomerulonephritis: II. Production of glomerulonephritis in rats by means of auto-antibodies to kidney. Arch. Path., **40**:153, 1945.
15. Cavelti, P. A.: Studies on the pathogenesis of rheumatic fever. III. Cardiac lesions produced in rats by means of autoantibodies to heart and connective tissue. Arch. Path., **44**:13, 1947.
16. Cavelti, P. A.: Autoantibodies in rheumatic fever. Proc. Soc. Exper. Biol. & Med., **60**:376, 1945.
17. Boorman, K. E., Dodd, B. E., and Loutit, J. F.: Hemolytic ecterus (alcholuric jaundice) congenital and acquired. Lancet, **250**:812, 1946.
18. Lewis, J. H.: The isoantigenic properties of alcoholic extracts of brain J. Immunol., **41**:4, 1941.
19. Schwentker, F. F., and Rivers, T. M.: The antibody response of rabbits to injections of emulsions and extracts of homologous brain. J. Exper. Med., **60**:559, 1934.
20. Freund, J., Casals, J., and Hesmer, L.: Sensitization and antibody formation after injection of tubercle bacilli and paraffin oil. Proc. Soc. Exper. Biol. & Med., **37**:509, 1937.
21. Freund, J., and McDermott, D.: Sensitization to horse serum by means of adjuvants. Proc. Soc. Exper. Biol. & Med., **49**:548, 1942.
22. Freund, J., Stern, E. R., and Posani, T. N.: Isoallergic encephalitis and radiculitis in guinea pigs after one injection of brain and mycobacteria in water-in-oil emulsion. J. Immunol., **57**:179, 1947.
23. Kabat, E. A., Wolf. A., and Bezer, E.: Studies on acute disseminated encephalomyelitis produced experimentally in rhesus monkeys. J. Immunol., **68**:265, 1952.
24. Fog, T., and Bardram, M.: Experimental disseminated encephalomyelitis and iridocyclitis in pigs. Nord. Med., **49**:851, 1953.
25. Bullington, S. J., and Waksman, B. H.: Uveitis in rabbits with experimental allergic encephalomyelitis. Arch. Ophth., **59**:435, 1958.
26. Suie, T., and Taylor, F. W.: Unpublished data.
27. Suie, T., and Dodd, M. C.: An immunologic study of rabbits sensitized with homologous uveal tissue. Am. J. Ophth., **39**:377, 1955.
28. Collins, R. C.: Experimental studies on sympathetic ophthalmia. Am. J. Ophth., **32**:1687, 1949.
29. ———: Further experimental studies on sympathetic ophthalmia. Am. J. Ophth., **36**:150 (July Pt. II), 1953.
30. Naquin, H. A.: An unsuccessful attempt to produce hypersensitivity to uveal tissue in guinea pigs. Am. J. Ophth., **39**:196 (Feb. Pt. II) 1955.
31. Suie, T.: Unpublished data.
32. Alvord, E. C.: Distribution and nature of the "antigen" responsible for experimental meningoencephalomyelitis in the guinea pig. Proc. Soc. Exper. Biol. & Med., **67**:459, 1948.
33. Jervis, O. A., and Koprowski, H.: Experimental allergic encephalomyelitis. J. Neuropath. & Exper. Neurol., **7**:309, 1948.
34. Cavelti, P. A.: Autoimmunologic disease. J. Allergy, **26**:95, 1955.
35. Landsteiner, K., and Chase, M. W.: Studies of the sensitization of animals with simple chemical compounds. J. Exper. Med., **71**:237, 1940.

MODIFIED BURCH TYPE EVISCERATION WITH SCLERAL IMPLANT

A. D. Ruedemann, Jr., M.D.
Detroit, Michigan

Adequate surgical treatment of a useless or badly damaged eye with little or no vision has long been a problem for all ophthalmologists. Since the first days of enucleation and enucleation procedures, surgeons have attempted to improve on the otherwise abnormal condition of the socket which results from removal of the eyeball or its contents. The hazards of sympathetic ophthalmia or hidden malignancy have always been points for serious consideration. Over a period of more than 100 years ophthalmologists have argued over the procedure offering the patient the greatest safety and the most acceptable cosmetic result. This paper will attempt to present the value of evisceration as a procedure offering safety, cosmosis and simplicity to a majority of patients.

Definition

1. Evisceration entails removal of all intraocular contents either (a) with cornea retained, or (b) with cornea removed. The eviscerated ocular contents may be replaced

with a scleral implant or no implant.

2. Abscission—removal of the anterior segment, leaving the posterior ocular segment intact.

3. Enucleation—removal of the eyeball within Tenon's capsule with or without placement of an intra-Tenon's prothesis.

Historical

Apparently the first case of extirpation of the eye was recorded by Bartisch[1] in 1583. Bartisch extirpated the contents of the whole orbit with a cutting spoon. This was a most severe operation and was only performed under circumstances of the direst necessity. In the days of no anesthesia, little or no asepsis, and poor control of hemostasis, the patient was often seriously endangered either by the procedure or its postoperative complications. Even under these circumstances enucleation was carried out in a similar manner with only small variation in instrumentation until the 1840's when Ferrall[2] in 1841, Bonnet[3] in 1841, and Stoeber[4] in 1842 independently suggested the removal of the eyeball from within Tenon's capsule.

In 1817, James Beer[5] was credited with the first evisceration. In attempting iridectomy for hemorrhagic glaucoma, the patient had an expulsive hemorrhage and the contents of the globe were removed. MacKenzie[6] reported a case of Butter's in his *Treatise on Diseases of the Eye*. In Butter's procedure the lens and vitreous were scooped out in an attempt to save the eye following intraocular foreign body. The eye was enucleated later (a single case). Barton, in 1837, suggested making a large corneal flap using a knife which was then extended into the lens and vitreous to encourage their extrusion. This method was used to stimulate the extrusion of percussion caps buried in the eyeball. If the cap would not present itself, the cornea was cut away with scissors.

Wardrop,[7] in 1834, mentioned a treatment for ophthalmia in horses. They apparently developed a sympathetic disease associated with suppuration in one eye. Veterinarians had noted that if the suppurating eye burst, the sympathetic involvement of the nonafflicted eye did not develop. They recommended burning out the involved eye with lime or a nail puncture. Wardrop suggested removing the cornea and squeezing out the lens and vitreous in humans as a treatment for sympathetic ophthalmia.

Apparently Noyes[8] was the first actually to perform evisceration as a routine procedure. In 1874, he published an account of a procedure which he used in cases of suppuration of the eye which produced good cosmetic effect and no sympathetic ophthalmia. Essentially his procedure was to incise the cornea and wipe out the eyeball. In 1878, Williams[9] presented a paper before the American Ophthalmological Society, suggesting that a good treatment for sympathetic ophthalmia in sloughing eyeballs was to scoop out the contents of these degenerating globes (one case with ossification of choroid).

In 1884, Alfred Graefe[10] deliberately performed an evisceration in order to prevent meningitis. Bunge,[11] a protege of Alfred Graefe, reported on 240 eviscerations performed by the master in which there was no sympathetic ophthalmia or death. Bunge later reported to the author of Norris and Oliver's[12] that in 500 cases there had been no death. The author of this portion of the text also noted that he was more partial to evisceration than formerly.

Mules[13] in the same year, 1884, performed evisceration for the prevention of sympathetic ophthalmia. His procedure was remarkable in that he introduced a hollow glass ball into the scleral cavity (without cornea). There was some objection to the procedure in that extrusions were claimed.

In 1886, Adams Frost[14] suggested enucleation of the eye with the placement of a glass ball in Tenon's capsule.

It was about this time that H. Knapp[15] noted that he practiced evisceration routinely until one case of orbital cellulitis caused him to switch to other procedures.

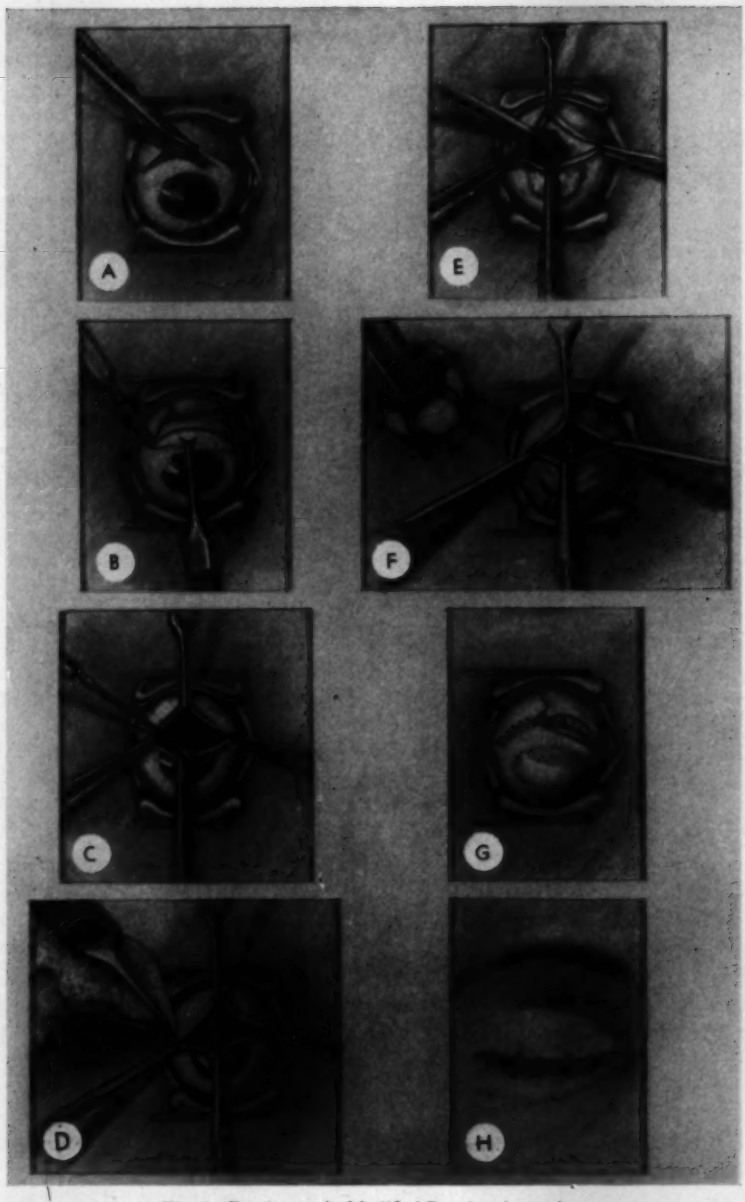


Fig. 1 (Ruedemann). Modified Burch evisceration.

(A) Stevens scissors section of conjunctiva and Tenon's anterior to superior rectus and from the 10- to 2-o'clock position to the sclera.
(B) Graefe knife section at the 10- to 2-o'clock position through the sclera.
(C) Iris repositor to separate uveal tract from sclera in suprachoroidal space.
(D) A 4.0 by 4.0 sponge is used to wipe out intrascleral debris and clean socket.
(E) A three-percent iodine swab is used to cauterize scleral interior.
(F) Placement 18-mm. KLF ball.
(G) Closure of sclera with running-locking stitch. The conjunctiva is similarly closed.
(H) Two lid sutures in place.

In 1900, Gifford[16] recommended a simple evisceration. His procedure was essentially a horizontal corneal incision with removal of the intraocular contents. If a Mules type procedure was not desired he made a cut through the sclera one-eighth inch above the cornea after a peritomy. The scleral cut was closed over with a conjunctival purse-string suture drawn over the cornea and when the conjunctiva retracted an insensitive cornea was noted.

Grimsdale and Brewerton,[17] in 1907, proposed that the cornea should *not* be amputated and proposed a long curved incision above the cornea through which the evisceration be performed.

Beard[18] in his textbook noted that he had somewhat better results with a vertical corneal incision and removal of the intraocular contents. He recommended evisceration for all cases except those with sympathetic ophthalmia, advanced phthisis bulbi and neoplasm.

Fox,[19] in 1910, in his textbook noted that he had performed 425 Mules procedures in 15 years without one case of sympathetic ophthalmia.

Gifford[20] reported 14 cases of sympathetic ophthalmia after Mules operation, nine after evisceration and three after the Frost-Adams procedure. A review of these cases does not indicate one single case of proven sympathetic ophthalmia. Even Brobst's case[21] was a boy 10 years of age who cut his eye while skinning a muskrat! The evisceration procedure (less than 12 hours after the injury) was not described and no pathologic study was made. Actually the boy developed an optic neuritis which resolved.

Sanders[22] mentioned a Negro in his 20's who had an evisceration plus enucleation procedure one week following a fall which ruptured his globe. Although the scleral stump contained sympathetic granulomatous tissue, apparently the actual surgical procedure was not well described.

To go back a bit, by 1898 the furor over enucleation versus evisceration had reached such heights that the Ophthalmological Society of the United Kingdom appointed a committee to consider the relative value of simple excision and the operations substituted for it. Beginning on page 233 of the *Transactions* of the society for 1898 is a report which must be considered a classic for its own or any other time.[23] In this particular report the committee collected evidence considering simple excision of the eyeball from Tenon's capsule, evisceration with or without the insertion of an artificial globe, the insertion of an artificial globe into Tenon's capsule after the removal of the eyeball, abscission, optical ciliary neurotomy, optical ciliary neurectomy.

Without considering all the details of this report, which covers over 70 pages, the conclusions noted indicated that simple extirpation of the globe within Tenon's capsule with or without the placement of a glass ball was the most acceptable procedure. In this procedure they noted in retrospect that there was not one case of a proven sympathetic ophthalmia. The optical ciliary neurectomy and neurotomy were generally not recommended. The report was signed by W. Adams Frost, chairman; Arthur H. Benson, Ernest Clark, John Griffith, Priestley Smith, and E. Treacher Collins.

This report was not universally accepted. In fact, a Dr. Thomas H. Bickerton would not sign the majority report. He thought that excision was too strongly advocated and the claims of simple evisceration were not sufficiently recognized and emphasized. He felt that more should not be removed than absolutely necessary and that this was a basic surgical tenet which was violated by enucleation. Bickerton followed with a minority report. He felt excision only necessary in and adoption should be limited to (1) intraocular and orbital malignancy, (2) extensively lacerated or contused wounds of the sclerotic, (3) markedly shrunken globes, (4) cases where sympathetic ophthalmia is already present. Even today this report must be considered seriously.

The *Transactions* for the International Congress of Ophthalmology in 1900 appar-

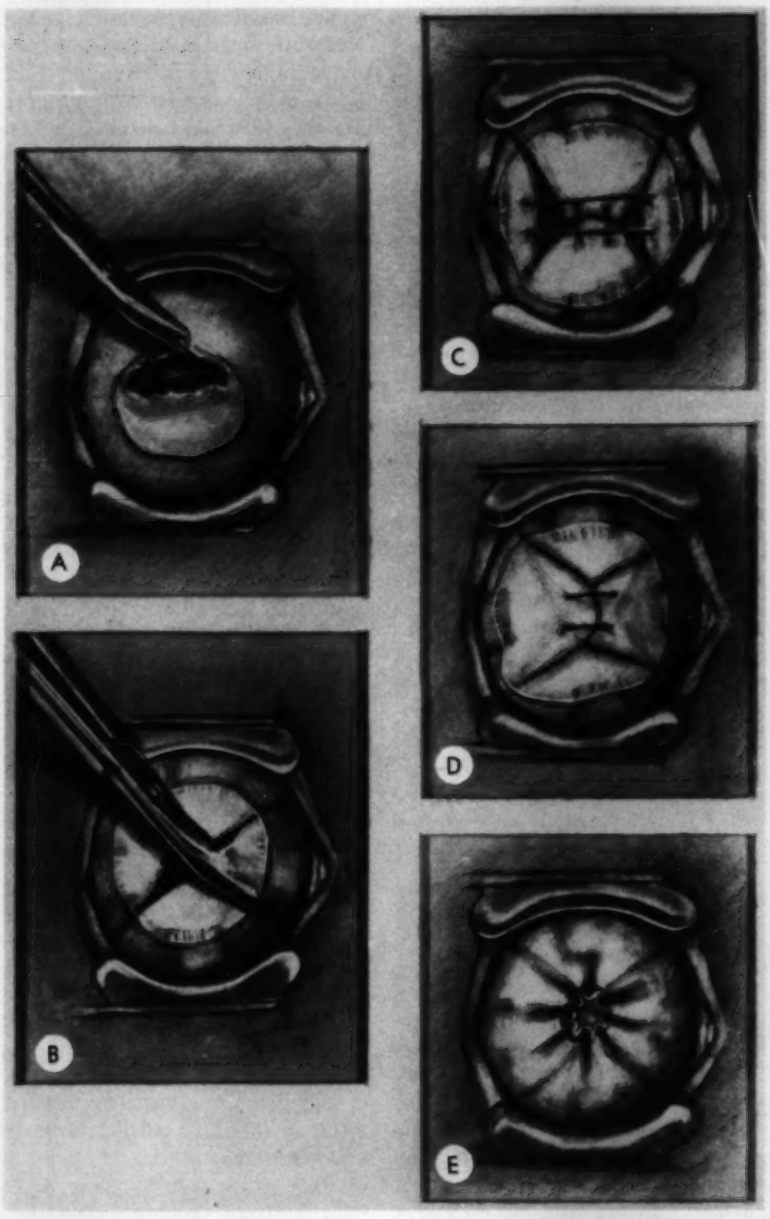


Fig. 2 (Ruedemann). Repair after postevisceration scleral or corneal rupture.
(A) Removal of necrotic tissue by scissors and forceps.
(B) Quadrantial section of sclera between rectus insertions.
(C) Overlapping closure of scleral section with double-armed horizontal mattress 3-0 catgut sutures.
(D) Final closure of scleral section.
(E) Pursestring suture of Tenon's and conjunctiva with 3-0 plain catgut.

ently contained another committee report suggesting enucleation as a preferred procedure over evisceration. Reports given at the International Ophthalmological Congress at Heidelberg in 1908 were in the same vein. (Neither report was available for study.)

In the same year, 1908, F. L. Henderson of St. Louis, in a speech delivered before the St. Louis Ophthalmological Society[24] entitled "Enucleation or evisceration?" made a strong plea for evisceration. He presented a case of a child who had a traumatic injury in which he was sure that an evisceration would have been a more satisfactory procedure. However, he stated that the weight of authority would indicate an enucleation as affording greater security against the development of sympathetic ophthalmia in the other eye. He felt that evisceration was a simpler procedure to perform and just as safe as enucleation.

The problem of evisceration versus enucleation smoldered along through the ensuing years until 1939, when Burch presented a paper on evisceration at the annual meeting of the American Ophthalmological Society.[25] In the procedure presented in this paper, Burch outlined a surgical technique which is the true forerunner of the one to be presented in this surgical series. Burch presented a series of 26 cases performed over a period of 35 years in which he had no evidence of difficulty. He claimed excellent cosmosis and general comfort, little irritation and accumulation of secretion, no sunken globe or loss of lid fold, with unusually good motility with a prosthesis.

His procedure was essentially an evisceration with retention of the cornea. A peritomy was made followed by a superior scleral incision and removal of intraocular contents followed by closure of the scleral incision with white silk and closure of the conjunctiva with black twisted silk. He claimed a moderately severe tenonitis followed for several weeks postoperatively. Interstitial vascularization of the cornea occurred usually. He noted only one scleral separation necessitating the removal of the glass ball.

This excellent presentation apparently created little interest in the evisceration technique in any form. Nothing further was heard of evisceration as a surgical procedure until 1956 when Berens[26] presented a paper entitled "Experience with a steel-mesh capped hollow plastic implant" in which he, George Z. Carter, and Arnold S. Breakey reported on a series of 144 cases of evisceration (performed by a number of different surgeons) utilizing this type scleral implant with removal of the cornea. The procedure is essentially a Mules type procedure with a special implant. Berens reported no cases of sympathetic ophthalmitis in his series. He noted extrusion in only five cases of the first 100 cases.

Dr. A. D. Ruedemann, Sr.,[27] reported a series of over 200 cases dating from 1939 in which no sympathetic ophthalmia was noted and there was surgical success in 95 percent of the cases. During this period and the ensuing months, there were several meetings of a prosthetic group, The American Academy of Ophthalmic Prosthetists. They reached the general conclusion that evisceration was a procedure to be preferred over enucleation for optimum cosmetic result.

It should be noted that in the years following the introduction of the plastic implant with enucleation by Ruedemann[28] there have been many variations of form and type, all attempting to get motility and cosmosis for an enucleated socket. The general disenchantment with the results has caused the ophthalmic surgeon to turn toward procedures that were not only safe but gave the patient a better cosmetic result.

At the American Academy of Ophthalmology and Otolaryngology meeting in October, 1958, Dr. Wendell Hughes presented a movie illustrating his technique for evisceration which would appear to be essentially a Burch procedure with the incision behind the insertion of the superior rectus muscle.

Method

The procedure to be outlined below is essentially a Burch procedure with modifica-

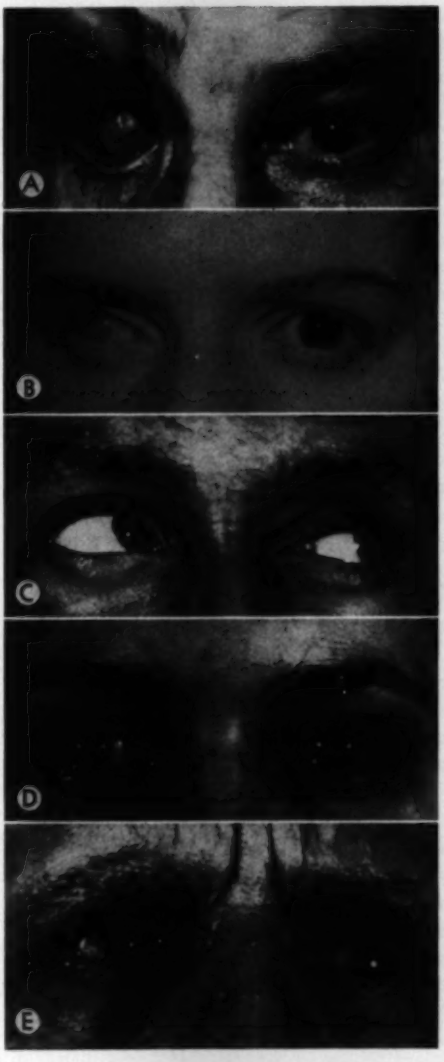


Fig. 3 (Ruedemann). Postoperative photographs.
(A) Male (40's) evisceration right eye. Notable intracorneal vascularization. Quiet socket.
(B) Female (20's) evisceration right eye. Intracorneal vascularization. Quiet socket.
(C) Male (30's) evisceration left eye, plastic shell.
(D) Male (30's) evisceration left eye, plastic shell.
(E) Male (40's) evisceration left eye, plastic shell.

tions. The series to be presented contains 150 cases drawn from our private office files taken from the years 1949 to 1958 (incomplete). Forty-eight cases from the Receiving Hospital files have also been taken in order to round out the series with cases treated shortly after trauma.

The procedure is as follows:

1. Adequate anesthesia, either local or general, with proper premedication and including hyponosis and analgesia.

2. The eye, cul-de-sacs and adnexa are carefully cleansed with soap and saline and copious saline irrigation.

3. A Burch lid spectrum is inserted between the lids and an incision is made with Steven scissors between the superior rectus muscle and the limbus, through conjunctiva and Tenon's capsule, exposing bare sclera. The incision is extended from the 10- to 2-o'clock positions. Excess blood is washed or wiped away and an incision with a Graefe knife is made from the 10- to 2-o'clock positions through the sclera into the vitreous cavity.

4. Hemostats are then placed in at least three positions around the scleral incision and the wound margins are held open.

5. An iris repositor is then inserted in the suprachoroidal space between sclera and choroid and the entire suprachoroidal space is swept, not only posteriorly but anteriorly, breaking the scleral spur and separating iris and ciliary body from the sclera and its attachments. By this method nearly the entire intracular contents can be removed in one piece and sent to the pathologic laboratory for evaluation.

6. Following the removal of the intraocular coats, vitreous and lens, the sclera is carefully wiped from within with 4.0 by 4.0-inch sponges inserted on heavy-duty pickup forceps. Moderate hemostasis is obtained and when the entire intrascleral coat appears clean the eye is carefully wiped dry and three-percent iodine solution is swabbed upon the entire intracorneal and scleral sur-

face. It is then copiously irrigated out with saline.

7. Using a Mules inserter, an 18 mm. lucite or KLF ball (rough surface) or an 18 mm. chromium cobalt stainless steel mesh-covered, microgrooved lucite ball is placed within the scleral cavity.

8. The scleral wound is then closed from the middle to each side using a 3-0 plain catgut double-armed suture which is first tied centrally and then, with a running-locking stitch, is carried to the 10- and 2-o'clock positions from the center. It is passed through conjunctiva and back toward the center, right and left, where it is tied. The cul-de-sacs are again carefully irrigated with saline and the lids are tied shut with two interrupted horizontal mattress sutures after an antibiotic ointment has been placed in the cul-de-sacs. No conformer is ever used.

The eye is dressed with an iced glove or a modified pressure dressing. Actually ice appears to have some beneficial effect on the chemosis which follows. The patient is returned to his bed on routine orders for analgesia and sedation as necessary. He is given freedom to roam. Usually antihistamines, are used, as well as intramuscular aqueous trypsin. The dressing is changed every other day, using an antibiotic ointment and a modified pressure dressing.

By the fifth or sixth day the moderate to marked conjunctival chemosis is reduced enough for the patient to go home. Often in the immediate postoperative period there is severe pain which is controlled by analgesia. By the end of the fifth day the pain has markedly subsided. The patient is usually sent home on antihistamines and local antibiotic ointment and told to keep the eye covered.

He is usually seen in the office by the end of one week at which time the conjunctival swelling is nearly all gone. There is usually some blood-staining of the cornea, as well as some early interstitial vascularization. The lid stitches have long since separated and the patient is noted to have good motility of an otherwise still moderately injected eye. By this time the patients may go without a patch if they desire and they may be sent to the prosthetist by the third week for the first fitting of a shell.

TABLE 1

NUMBER OF CASES

1948—(partial) 1958	
63	Males
87	Females

Contraction of the scleral coats usually continues over a period of approximately three months postoperatively by which time a full prosthesis allowing adequate clearance of the cornea is utilized. This prosthesis usually has a drainage hole below and the patient may wear this continuously without removal. There is remarkedly little irritation or secretion. Excellent mobility is obtained.

RESULTS

Table 1 indicates the number of cases in this series with division as to sex.

Table 2 indicates the age separation of the patients involved and has been divided categorically into the ages before 10 and after 10 years. This is because the usually accepted age for ultimate globular size is approximately nine years.

In Table 3 the cases are divided as to clinical diagnosis. It should be noted that one case of melanoma was eviscerated and two days later, when the pathologic diagnosis was obtained, enucleation of the scleral coat was performed. This patient has been followed for five years and to date is completely well, with the socket clean. There is one case of an expulsive hemorrhage following cataract extraction. Pathologic specimens revealed a hemangioma of the choroid.

TABLE 2

AGE

Years	Cases
Less than 10	23
Greater than 10	127

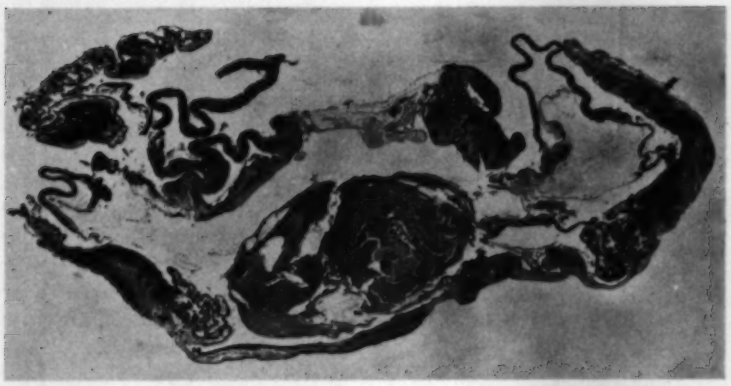


Fig. 4 (Ruedemann). Section in case of F. M., aged 25 years. Clinical diagnosis: Phthisis bulbi, hemorrhagic glaucoma. Pathology diagnosis (4531): No malignancy. (Kresge Eye Institute Pathology Laboratory, Dr. Windsor Davies.)

Fig. 5 (Ruedemann). Section in case of L. L., aged 70 years. Clinical diagnosis: Phthisis bulbi, diabetes. Pathology diagnosis (4404): No malignancy. (Kresge Eye Institute Pathology Laboratory, Dr. Windsor Davies.)

There are three cases of evisceration following trauma. The evisceration occurred five days, 32 days, and two months posttrauma.

Implant size is of some importance and is noted in Table 4 which indicates that the greater number of implants whether mesh or lucite are of the 18 mm. size. Since 1954, the lucite ball has been utilized almost exclusively.

Table 5 indicates the follow-up course of these patients. It should be noted that 37 were followed for less than one year; operations on 19 of these were performed in the year 1958 and many of the other cases were referred from outside the general area and have been followed by their local ophthalmologists. In not one of these cases has there been any indication of complication.

TABLE 3

CLINICAL DIAGNOSIS

Phthisis bulbi	65
Absolute glaucoma	52
Retrolental fibroplasia	8
Diabetic glaucoma	12
Congenital glaucoma	4
Melanoma	1
then enucleated—followed 5 years	
Congenital defect	2
Expulsive hemorrhage	1
Hemangioma by pathologic specimen	
Posttrauma (early)	3
(5 da., 32 da., 2 mo.)	
Lime burn	2

TABLE 4

IMPLANT SIZE

	Mm.	Cases
Mesh:		
	Less than 18	15
	18	19
Lucite:		
	Greater than 18	10
	18	67
	Less than 18	32
Unknown:		7

TABLE 5

FOLLOW-UP

Year	Cases
Less than 1	47
1	13
1–5	52
More than 5	38

TABLE 6

CHOICE OF OPERATION

Eviscerations	Year	Enucleations
10	1953	7
11	1954	16
16	1955	12
16	1956	8
12	1957	5
19 (to date)	1958	3
	Five Years	
1953–1958	Total eviscerations	84
1953–1958	Total enucleations	51

Table 6 is self-explanatory and shows the trend away from enucleation in the past five years.

Table 7 indicates the failures. In this series there were six cases out of 150. Actually not one of them can be considered a postoperative failure. It is obvious from the six failures to date that failure in none of them is surgical. The last one occurred because the patient insisted on removing her prosthesis to clean it and damaged her cornea. She was out of the city at the time and when she had returned her cornea had become necrotic, possibly due to continued use of local steroids without use of antibiotics. Even attempted repair was unsuccessful. The globe was then sectioned in a standard manner and the condition remained quiet to date.

It should be noted that, in those cases in which the ball must be removed because of exposure or the ball actually extrudes, the usual method of treatment is as follows:

After standard preoperative preparation and cleansing, a Burch lid speculum is inserted between the lids and the exposed ball is either removed or the scleral coats are opened to each side, allowing escape of the ball. Prior to making the scleral sections, the conjunctiva is incised circumferentially at the limbus along with Tenon's capsule. This exposes sclera and allows adequate section. The scleral coat is then incised (excluding Tenon's) on each side of the four rectus muscles extending posteriorly to the optic

TABLE 7

FAILURES

(Six of 150 = four percent)

1. 42-yr.-old male—18 mesh—out after 4 yr., 10 mo. —replaced and all right 1 yr. later.
2. 33-yr.-old female—16 mesh—removal 2 yr., 9 mo.—placement of 17 mm. lucite—all right 2 yr., 4 mo. later.
3. 5-yr.-old male—20 lucite—out after 2 yr., 8 mo.—extrusion with placement of 16 mm. mesh—all right after 9 mo.
4. 18-yr.-old female—20 lucite—out after 3 yr., 5 mo.—15 mm. mesh placed and over 1 yr. later still in place and all right.
5. 31-yr.-old female—18 lucite—out after 4 yr., 7 mo.—placement of 17 mm. mesh with conformer —no follow-up since.
6. 40-year-old female—17 lucite—out after 2 mo.—use of local steroids and injury to cornea—replaced with 13 mm. lucite—all right after 2 mo.

TABLE 8

PARTIAL RECEIVING HOSPITAL LIST

1949–1958	48 cases
1. Traumatic laceration	34
2. Phthisis bulbi—secondary to trauma	10
3. Congenital defect	1
4. Glaucoma—secondary to trauma	3

nerve. The scleral segments are then sewn together, using 3-0 plain catgut suture, and the Tenon's is plicated over, using an interrupted plain catgut suture. The conjunctiva is then closed with a running purse-string suture. The eye is dressed at this time with a conformer (because of foreshortening of the cul-de-sacs) and antibiotic ointment and a modified pressure dressing with or without lid sutures are applied.

Table 8, a partial listing of the Receiving Hospital cases, contains 48 cases, mostly of traumatic etiology. All of them were treated within a period of hours after trauma. They were not operated unless the eye appeared incontrovertibly lost and vision was no light perception.

Table 9 reviews the use of an 18 mm. sphere or steel mesh. Generally speaking, a sphere greater than 20 mm. is not satisfactory nor is a sphere smaller than 14 mm. The 14-mm. sphere is used only in children under 10 years of age; in fact, usually in children under two years of age.

Table 10 merely points out the inadequacy of the Receiving Hospital list but again these cases are included to show the use of evisceration in immediate posttraumatic cases.

TABLE 9

IMPLANT (Receiving Hospital)

Mm.	Cases
Plastic sphere	
18	25
More than 18	6
Steel mesh	
18	6
More than 18	1
Glass ball	
18	7
More than 18	2
None	1

TABLE 10

RESULTS* (Receiving Hospital)

Year	Cases
1949	5
1950	
1951	5
1952	10
1953	2
1954	3
1955	2
1956	
1957	16
1958	5

* Follow-up—1 known extrusion, 1 yr. postoperative—no replacement.

(To date there is only one known extrusion in this series and in the entire series there is not one case of sympathetic ophthalmia or even sympathetic irritation.)

DISCUSSION

The arguments against evisceration are summarized in Table 11.

1. *The problem of sympathetic ophthalmia.* To date no proven case of sympathetic ophthalmia has been uncovered in the literature following a true evisceration procedure. In several questionable cases where sympathetic ophthalmia followed an evisceration procedure there was notable uveal contents remaining within the scleral coats. In some cases in which sympathetic ophthalmia appeared to follow within the prescribed time following evisceration, the allowable safety period had long since passed or evidence of the disease was already present.

2. *The long postoperative course has been noted and considered.* With the end-results

TABLE 11

ARGUMENTS AGAINST EVISCERATION

1. Sympathetic ophthalmia
2. Long postoperative course
3. Small stump (if no implant)
4. Extrusion common
5. Malignancy
6. Contraction of scleral coat
7. Comparative rotation—old time measurement of evisceration without ball (Hotz, Truc, deSchweinitz) indicated no better movement—not true with ball implant.

involved it hardly seems to have merit as an argument against evisceration.

3. *The problem of a small stump is obvious if there is no implant.* However, in the procedure just described an implant is used routinely. The stump is of normal size. As a matter of fact, the size of the eye is normal, with only slight contraction and a prosthesis is cosmetically effective.

4. *Extrusion is not common.* In this series of 150 cases plus the 48 Receiving Hospital cases there were only seven cases of extrusion and none of these were in the early postoperative course.

5. *Malignancy.* One case of malignancy has been discovered in this series and was operated by removal of the scleral coats within several days of the original evisceration procedure. In this case a five-year follow-up shows no evidence of recurrence of the tumor. It should be noted at this time that in most of the cases in this series no tumor was evident. In a number of the enucleations reviewed in conjunction with this series, over 10 melanomas were discovered —prior to surgical procedure. Obviously, melanoma is more easily discovered than missed.

6. *Contraction of the scleral coat.* In the old evisceration without placement of scleral implant, the contraction of the scleral coat meant a markedly reduced scleral stump, necessitating a large reform prosthesis. This definitely reduced the advantage of the evisceration procedure. However, it must be noted that this is of definite advantage in the presently described procedure, for some contraction of the scleral coats is actually necessary to reduce orbital volume and allow utilization of a three-dimensional anterior segment. This gives the patient a very real appearance when the prosthesis is observed from the side or the front. If some contraction is not obtained, then this type of prosthesis is difficult to utilize, since the orbital volume is so great that only a contact prosthesis may be used (in order to obtain adequate corneal clearance).

Corneal clearance is of some importance because of the definite reduction in corneal sensitivity noted as a general feature of these cases. The patient is usually unaware of any difficulty with the prosthesis in the early days and should be checked at regular intervals in order that corneal erosion does not occur.

Several cases have developed central corneal erosion in the first few postoperative weeks. This is due to enthusiasm with the new prosthesis and obvious lack of care in controlling ocular motility. If the corneal clearance is not satisfactory, a rubbed area will develop and this may cause severe corneal erosion.

One case of this type was noted in a man, a plasterer for the Detroit Public Schools. After he had obtained his prosthesis, he immediately returned to work. A foreign body became embedded beneath the prosthesis during the course of his very dusty duties and caused corneal erosion. This was discovered within a few days of its occurrence and was controlled with local antibiotics. He has been followed for over a year and a half since this time and at present the condition is controlled and the result completely adequate.

7. *Comparative rotation.* In early reports of measurement of eye movements after evisceration without a ball, several authors indicated no improvement. If a scleral implant is used, however, the movements are much superior to any obtainable with the glass ball in Tenon's or with most of the generally unsuccessful intra-Tenon's implants.

8. *Sloughing of the sclera.* The old arguments about sloughing of the sclera have not been noticed in this series. There was only one case where trauma was an obvious factor and local steroids had been used routinely.

9. *No prolonged hospitalization.* In this series, the average hospital stay was approximately five days.

10. *Escape of the artificial globe* has been

noted in only seven of 198 cases and none of these was during the immediate postoperative period. In at least half of these cases, there was some good reason for rupture of the sclera with exposure of the implant. Jardon believes that this occurred because the prosthesis was made too tight for the scleral and corneal coats and caused contact erosion. He feels that it is important (1) to use a 17- or 18-mm. ball, (2) to use lucite or chromium cobalt stainless steel mesh over grooved lucite or KLF with *no* postoperative conformer and (3) to be sure of careful fitting of the prosthesis to assure corneal clearance. There has been no question about breakage of this unbreakable plastic material or any real difficulty with intolerance. As a matter of fact, there is remarkable freedom from symptoms and few complaints of pain in the socket or other discomfort.

11. *The amount of secretion and conjunctival irritation* with an evisceration is markedly less than with enucleation or with the various implants. The patients generally do not require removal of their prostheses nor is it recommended. Washing the cul-de-sacs with saline or boric acid solution is adequate to remove excess secretions. Even this does not need to be done routinely. The patient is advised to leave the prosthesis alone as much as possible.

12. *Pathologic material.* The argument about loss of pathologic material must be considered. In most of this series no attempt was made to preserve pathologic material. However, in some cases it was felt that the material might be of some interest to the pathologist. Recently, there has been routine evaluation of the intrascleral coats. Generally speaking, the pathologist has been satisfied with the material presented to him.

Finally, although there are many arguments for evisceration (table 12), it would be hard to improve the arguments of Bickerton in his minority report for the *Transactions* of the Royal Society of the United Kingdom for 1896. However, first to consider is the superior cosmetic result of evisceration over an enucleation procedure. There is no displacement of the implant through the muscle cone; there is much better motility of the globe; there is no sunken upper lid and the greater orbital volume allows a much lighter and a more readily utilizable prosthesis.

TABLE 12

ARGUMENTS FOR EVISCERATION

1. Cosmosis superior
   a. No displacement through muscle cone
   b. Better motility
   c. No sunken upper lid
   d. Greater orbital volume
2. Readily consent to surgery
3. Good motion
4. Burch felt operation as simple and safe as enucleation, Henderson simpler operation
5. Less irritation, lacrimation and secretion. More normal mucous membrane

Very important, too, in consideration of surgery for a useless eye which may become irritated and its retention dangerous to the patient is that it is much easier to accept a surgical procedure involving evisceration rather than enucleation which some patients absolutely reject. They more readily accept evisceration, knowing that the eyeball will remain.

Another consideration is good motility of the globe (with or without a prosthesis). This is obviously related to the maintenance of ocular volume, intraorbital volume, and the retention of the normal attachment of the muscles to the sclera.

Authors who have described evisceration have noted time and again the simplicity of the procedure. I certainly reiterate and emphasize their statements. Evisceration is a simpler, quicker, neater and as safe a procedure as enucleation.

Finally, without a doubt, evisceration causes less irritation, lacrimation, and secretion. This is most likely due to the retention of a normal mucous membrane and cul-de-sac area.

CONCLUSIONS

A series of 198 cases of modified Burch

evisceration has been presented. No case of sympathetic ophthalmia has been encountered. In one case of malignancy, there has been no recurrence five years postoperatively. The method, postoperative course, and results have been outlined. I agree wholeheartedly with others who believe this procedure is ideal when it is necessary to remove the irritable, traumatized, or blind painful eyes in which it is reasonably certain there is no malignancy. If removal of ocular contents becomes necessary in cases of intraocular infection or inflammation of a sympathetic nature, I see no reason why evisceration would not be a satisfactory procedure.

690 Mullett Street (26).

References

1. Bartisch, G.: Ophthalmodouleia oder Augendienst, 1583. Am. Encylop. Ophth., Chicago, Cleveland Press, 1915, v. VI, p. 4392.
2. Ferrall: Dublin J. Med. Sci., **19**:335, 1841. Ibid. p. 4393.
3. Bonnet: Ann. Ocul., **5**:27, 1841; **7**:39, 1842.
4. Norris, W. A., and Oliver, C. A.: System of Diseases of the Eye. Philadelphia, Lippincott, 1842, v. 3, p. 883.
5. Beer, J.: Graefe-Saemisch Handbuch Augenh., v. 3, p. 376; Am. Encyclop. Ophth., p. 4418.
6. Mackenzie: Treatise on Diseases of the Eye. London, Longman, 1834; Am. Encyclop. Ophth., p. 4418.
7. Wardrop: Morbid Anatomy of the Human Eye, 1834. Am. Encyclop. Ophth., p. 4418.
8. Noyes: Treatise on Diseases of the Eye. New York, William Wood, 1881, 189.
9. Williams, H. W.: Extirpation of the ossified choroid without enucleation of the eyeball. Tr. Am. Ophth. Soc., **2**:406, 1878.
10. Graefe, A.: Versam. Deutsch. Naturforscher, **3**:770-771 (Sept.) 1884; Am. Encyclop. Ophth., p. 4420.
11. Bunge: Mittheil aus der Univsitatsaugenklinik zu Halle, 1887. Encyclop. Ophth., p. 4389.
12. ———: Am. Encyclop. Ophth., p. 893.
13. Mules: Evisceration of the eye and its relation to the bacterial theory of the origin of sympathetic disease. Tr. Ophth. Soc. U. Kingdom, **5**:200, 1885; Brit. M. J., **1**:246, 1886.
14. Frost, A.: Middlemore Prize Essay, Brit. M. A. 1886. Tr. Ophth. Soc. U. Kingdom, **18**:236, 1898.
15. Knapp, H.: Case of evisceration of the eye, followed by (nonpurulent) orbital cellulitis (thrombosis) recovery. Arch. Ophth., **14**:309, 1885; Arch. f. Augenh., **16**:55, 1886.
16. Gifford: On strictly simple evisceration of the eyeball. Arch. Ophth., **29**:422, 1900.
17. Grimsdale and Brewerton: Textbook of Ophthalmic Operations, Chicago, W. T. Keener, 1907, p. 181.
18. Beard: Ophthalmic Surgery. Philadelphia, Blakiston, 1914, ed. 2, pp. 430-436.
19. Fox, L. W.: Diseases of the Eye. New York, Appleton, 1910, p. 527.
20. Gifford: On sympathetic ophthalmia after evisceration and Mules operation with a case. Ophth. Record, **17**:584, 1908.
21. Brobst, C. H.: Sympathetic ophthalmia following Mules operation. Ophth. Record, **17**:583, 1908.
22. Sanders, T. E.: Personal communication.
23. Report of a committee of the ophthalmological society appointed in March, 1896, to consider the relative value of simple excision of the eyeball, and the operations which have been substituted for it. Tr. Ophth. Soc. U. Kingdom, **18**:233, 1898.
24. Henderson, F. L.: Enucleation or evisceration? Am. J. Ophth., **25**:7, 1908.
25. Burch: Evisceration of the globe with scleral implant and preservation of the cornea. Tr. Am. Ophth. Soc., **37**:272, 1939.
26. Berens, et al.: Experience with a steel-mesh capped hollow plastic implant. Tr. Am. Ophth. Soc., **54**:337, 1956.
27. Ruedemann, A. D.: Evisceration with retention of the cornea. Tr. Am. Ophth. Soc., **54**:348, 1956.
28. ———: Plastic eye implant. Am. J. Ophth., **29**:947-952, 1946.

AN INITIAL EVALUATION OF (ARISTOCORT®) TRIAMCINOLONE IN THE THERAPY OF OCULAR INFLAMMATION*

PART I: EXPERIMENTAL STUDIES

SHANKAR B. CHAVAN, M.D., AND EDWARD J. CUMMINGS, M.D.
Washington, D.C.

In the short period of their existence as therapeutic agents, the search for newer products of the adrenal corticosteroids continues to provide us with improved topical and systemic cortical steroids for the treatment of various ocular inflammations and allergic states. The analogs, predisone and prednisolone, were found to be superior to cortisone and hydrocortisone.[20, 28] Experimental studies on uveitis revealed that a given anti-inflammatory response required doses several times greater of cortisone or hydrocortisone than of prednisone or prednisolone.[28, 32] As reported previously in the literature by several authors,[1, 2, 29, 37, 44, 47] the simultaneous administration of corticosteroids, antibiotics or antihistaminics exerts an ameliorating influence on the course of many ocular infections and allergic reactions.

Further research and clinical analysis of newer compounds are constantly being carried out to evaluate their efficacy, potency, and toxicity in the treatment of ocular inflammation for short or long-term therapy. One of the most recent adrenal steroids is triamcinolone, which has been shown to be a more potent and less toxic corticosteroid. A special derivative of triamcinolone free alcohol (Aristocort®), known as triamcinolone acetonide, has recently been shown to be very active topically. Clinical studies indicate that 0.1-percent triamcinolone acetonide, topically, has an activity equal to or greater than 1.0-percent hydrocortisone.[23, 36, 43] It is the purpose of this report to introduce these new preparations in the field of ophthalmology.

* From the Eye Research Section, Department of Surgery, Georgetown University Medical Center. The research fellow in ophthalmology (Dr. Chavan), has been supported by the Lions (22-C) Eye Bank and Research Foundation, Washington, D.C. The research related to this study was supported in part, and the triamcinolone (Aristocort) preparations supplied, through the courtesy of Dr. Christopher H. Demos, Medical Research Section, Lederle Laboratories, a division of American Cyanamid Co., Pearl River, New York.

PAST STUDIES

These newer synthetic corticosteroids differ from cortisone, hydrocortisone, prednisone and prednisolone in that they possess a hydroxyl group at the 16 position and a fluorine at the 9 carbon position. The free alcohol preparation is delta[1]-9-alpha-fluoro-16 alpha-hydroxy-prednisolone. The acetonide grouping is attached to the 16 and 17 carbon atoms (fig. 1).

These changes were achieved as the culmination of a search for a corticosteroid with increased glucocorticoid and greatly diminished mineralocorticoid activities.[4, 5] Glucocorticoids have to do principally with carbo-

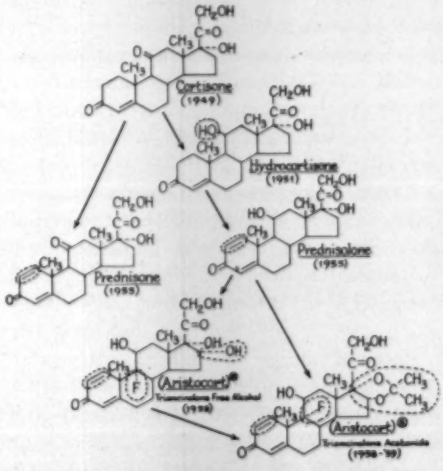


Fig. 1 (Chavan) and Cummings). Chemical structure of six adrenal corticosteroids. Note that the change from preceding compound is indicated in interrupted circles.

hydrate metabolism, a function which is correlated with anti-inflammatory activity; the mineralocorticoids have to do principally with electrolyte and water metabolism.

Laboratory and clinical studies have shown that the addition of fluorine at the 9-alpha position greatly increases the glucocorticoid activity. Clinical use is limited, however, because of marked sodium and water retention, hypertension and negative potassium, calcium and nitrogen balance with other steroids.[9] Laboratory[34] and clinical evidence thus far with triamcinolone indicates no sodium or water retention. This advantage is attributed to the addition of the hydroxyl radical at the 16-alpha position.[4, 5, 18, 22, 25, 49]

With the creation of triamcinolone, previous corticosteroid therapeutic ratios, that is potency versus side-effects, have been widened at both ends to provide these advantages: (1) equivalent anti-inflammatory and anti-allergic benefits with dosages averaging at least one-third less than prednisone or prednisolone, particularly in dermatologic and allergic conditions;[15, 16, 26, 31, 40, 41, 42, 48] (2) freedom from sodium and water retention;[13, 15, 26, 30, 31, 35, 45] (3) absence of potassium depletion in the usual clinical doses;[35, 45] (4) psychic equilibrium rarely disturbed;[11, 30, 39, 40, 42] (5) low incidence of osteoporosis with compression fracture,[39, 45] and little or no increase in blood pressure.[16, 19, 30, 41, 42]

Triamcinolone has now been studied intensively and extensively for substantial periods up to more than one year in patients with rheumatoid arthritis;[6, 8, 18, 21, 24, 45] in conditions such as chronic asthma and allergic rhinitis;[15, 16, 19, 39, 40] psoriasis and other dermatoses of allergic and inflammatory origin including atopic dermatitis, exfoliative dermatitis, pemphigus, dermatitis herpetiformis, eczematoid dermatitis, contact dermatitis and angioneurotic edema;[3, 26, 27, 30, 31, 33] disseminated lupus erythematosus;[12, 13] and thrombocytopenic purpura;[11] and the nephrotic syndrome.[23] Doses of triamcinolone equivalent to, or somewhat less than prednisone or prednisolone, have been therapeutically effective in rheumatoid arthritis. In allergic and dermatologic diseases, however, triamcinolone is about twice as active as the other steroids.

Triamcinolone acetonide and its parent compound, triamcinolone free alcohol, given orally in rheumatoid arthritis patients indicates that the acetonide has approximately the same antirheumatic activity as does the free alcohol. Toxicity studies in rats do not show any unusual toxicity for triamcinolone or its acetonide over what would be expected from a potent steroid in the doses in which it was administered.[10] Double-blind investigations reveal that a topical preparation of the triamcinolone acetonide (0.1 percent) is 10 times as active as hydrocortisone (one percent) in various types of dermatoses.[10, 43]

The present investigations were carried out in two parts: first, experimental studies on induced uveitis in rabbits in which triamcinolone free alcohol was compared to cortisone, hydrocortisone, corticotropin (ACTH), and prednisolone; and second, a clinical study of triamcinolone free alcohol orally and triamcinolone acetonide topical preparations in the treatment of ocular inflammations,* to verify the presumption that these preparations are as effective as, or more potent than, available steroid preparations.

Laboratory studies of experimental uveitis

The rationale of corticosteroid therapy described by Duke-Elder[14] cited by Abrahamson and Abrahamson[2] for the adrenocortical steroids explains the action in terms of "a temporary blockage of the exudative phase of inflammation and an inhibition of fibroblastic formation in the process of tissue repair, whether the cause of the disease is bacterial, anaphylactic, allergic, or traumatic."

An initial evaluation of the anti-inflammatory effects of triamcinolone free alcohol was

* Part II, of this article will appear later, separately.

based on the results of three animal experiments. The first two were carried out by comparing the drug with cortisone, hydrocortisone, corticotropin (ACTH) and prednisolone, while the third was done to test the triamcinolone free alcohol activity at various dose levels.

Two types of ocular inflammatory lesions were induced in the animals' eyes, one a moderate type and the other a severe type of uveitis. A modification of the technique of Foss,[17] Vogel and Leopold,[46] and O'Rourke[32] was employed to induce uveitis of a moderate type in order to evaluate the blocking effects of prophylactic therapy comparing various steroids administered prior to the induction of activity in experimental animals (Experiment 1). This was achieved by reducing the time interval between the sensitizing injection of horse serum and the shocking dose injection of the same antigen intravitreously. However, the technique for producing lesions of severe uveitis activity was done (Experiments 2 and 3) by following the method of Schlaegel and Davis,[38] and O'Rourke, et al.[32] This method was achieved by increasing the time interval to four weeks between the sensitizing and shocking dose of antigen. The only modification was to instill an antibiotic prior to the shocking dose and the use of a special needle to inject the antigen.

All the animal eyes were observed each day by slitlamp and ophthalmoscopic examination and a notation was made of the character and intensity of the uveitis lesions. The chemosis of the bulbar conjunctiva was not graded because of its proximal relationship to the injected area; however, vitreous haze or opacities may be graded because of their relationship to the intraocular inflammation.

Five features of the resulting intraocular inflammatory lesions were seen and graded: (1) Vascularization of the albino iris with posterior synechias, (2) aqueous flare and cellularity in the anterior chamber, (3) cell deposits on the endothelial surface of the cornea (keratic precipitates), (4) inflammatory fibrinous exudates in the pupillary area and on the anterior surface of the lens, (5) vitreous haze or opacities. On these criteria, the severity of the total lesions of the groups was graded from 1 to 4+ daily. Figures 2a and 2b, 3, 4, and 5 demonstrate the results of these experiments and each point represents the total (+) activity of six eyes charted against time.

Fig. 2A (Chavan and Cummings). Experiment 1. A typical moderate type of horse serum uveitis response in experimental rabbit eye (control group) was obtained 72 hours after intravitreous injection of the antigen, using a special sterile nonpyrogenic disposable Monoject 27-gauge needle. Moderate intraocular inflammatory lesions were seen by slitlamp and ophthalmoscopic examination. A modification of the technique of Foss, Vogel and Leopold, and O'Rourke, et al., was employed.

Experiment 1

Comparative blocking effects of corticosteroids for prophylactic therapy

The comparative anti-inflammatory blocking effects of corticosteroids for prophylactic therapy were studied by restricting the treatment to 48 hours prior to the induction of uveitis lesions. Eighteen full-grown albino rabbits with normal eyes were sensitized to 10 cc. undiluted horse serum (Lederle) by

Fig. 2B (Chavan and Cummings). Experiments 2 and 3. A near-severe type of horse serum uveitis in experimental rabbit eye (control group) was obtained at 72 hours after intravitreous injection of the antigen, using a Monoject 27-gauge needle. Rather severe intraocular inflammatory lesions were seen by slitlamp and ophthalmoscopic examination. A modification of the technique of Schlaegel and Davis, and O'Rourke, et al., was employed.

subcutaneous injection beneath the shaved abdominal skin according to the technique of Foss,[17] Vogel and Leopold,[46] cited by O'Rourke and associates.[32] On the 12th day the animals were divided into six groups of three each, and each group was treated with a prophylactic dose of steroid by injection intramuscularly, giving the highest dosage level (that is, highest mg./kg. of body weight) according to the plans (table 1) previously employed in the experimental studies of steroid therapy by several authors.[7, 32, 47] As a test of its potency, the triamcinolone free alcohol dosage was held to a level one-tenth that of the cortisone and hydrocortisone and one-half that of prednisolone.

These injections were repeated on the 13th day and on the 14th day of this experiment; all the animals were anesthetized with intravenous pentobarbital (Nembutal, 25 mg./kg. of body weight) and the procedures were performed under sterile conditions and local anesthetic solution (sterile pontocain 0.5-percent solution was instilled three times at intervals of three minutes each) and the eye speculum was inserted. The eye was irrigated with sterile normal saline and an antibiotic solution, containing neomycin, polymyxin B, and Gramicidin,* was instilled and a shock dose of 0.1 cc. of the same horse serum was injected intravitreously through the superior-temporal pars-plana region of each eye, using a special sterile nonpyrogenic disposable Monoject 27-gauge (three-eighths inch bevel intermediate) needle† and tuberculin syringe. All the animal eyes were observed each day by slitlamp and ophthalmoscopic examination and the five features subsequently resulting from ocular inflammation were graded.

* Neosporin® ophthalmic solutions was supplied through the courtesy of Dr. E. N. Whitman of Burroughs-Wellcome Co., Tuckahoe, New York.

† Roehr Products Co., Inc., Waterbury, Connecticut.

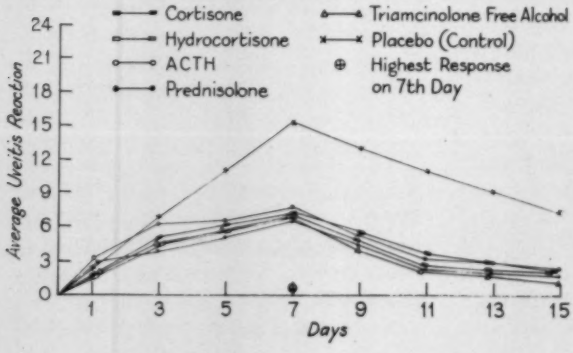


Fig. 3 (Chavan and Cummings). Graph of results in comparative prophylactic steroid blocking effects on uveitis lesions in rabbit eyes.

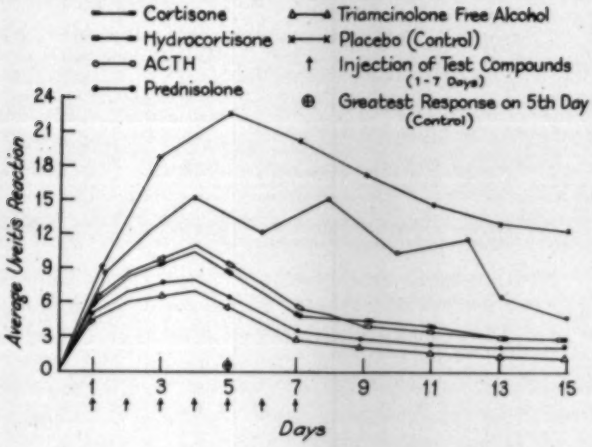


Fig. 4 (Chavan and Cummings). Graph of results in comparative steroid therapy in established uveitis lesions in rabbit eyes.

Results. The uveitis activity in the control eye reached its maximum peak on the seventh day after the injection of shocking dose of antigen intravitreously, and at this stage there was a great difference between the control and treated eyes. The response evoked in the control eyes compared to that of treated eyes was noteworthy (figs. 2a, and 3) being much more severe in the control eyes. The inflammatory activity in the treated eyes was definitely of a moderate degree in all eyes, but in none of them did the prophylactic therapy completely block the onset of the lesion activity, except that a complete blocking effect was a striking example in one out of three of the triamcinolone free alcohol group. Over all, the suppressive influence and superiority of triamcinolone free alcohol given in one-tenth the dose was equivalent to the level of cortisone and hydrocortisone and one-half the level of prednisolone dosage.

During the first seven days of the experiment the results were comparable to those of previous authors.[32] The uveitis response in the prophylactically treated eyes was much less than the control eyes, which appears to indicate a definite influence of suppression of these drugs on experimental uveitis activity with a tendency for the activity to be much less pronounced. There is confirmation of the previous observation that the prophylactic therapy does not have any definite influence

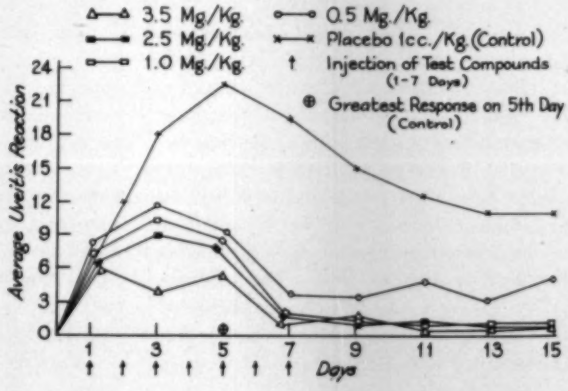


Fig. 5 (Chavan and Cummings). Graph of results, showing various dosage level effects of triamcinolone free alcohol, in established uveitis in rabbit eyes.

TABLE 1

PLANS FOR DOSAGE SCHEDULE FOLLOWED IN EXPERIMENTS I AND II*

Group No.	Treatment	Daily Dose (intramuscular)	Human 70 Kg. Equivalent Dosage and Potency Level	Remarks
1	Cortisone acetate (Cortone acetate, Merck)	25 mg./kg.	1750 mg.	Required very high dosage level
2	Hydrocortisone sodium succinate (Solu-Cortef, Upjohn)	25 mg./kg.	1750 mg.	Required very high dosage level
3	Prednisolone 21-phosphate (Hydetrasol, Merck)	5 mg./kg.	350 mg.	Required ½ less dosage level than cortisone and hydrocortisone
4	Triamcinolone free alcohol (Aristocort, Lederle)	2.5 mg./kg.	175 mg.	Required 1/10th less dosage level than cortisone and hydrocortisone and ½ less dosage level than prednisone or prednisolone
5	Corticotropin (ACTH, Armour)	10 units/kg.	700 units	Required higher dosage level
6	Placebo (normal saline)	1 cc./kg.	70 cc.	Control group

* Based upon the previous studies on cortisone and hydrocortisone by Biegel,[7] corticotropin (ACTH) by Woods,[47] and prednisone by O'Rourke and associates.[32] Triamcinolone free alcohol, by contrast was administered in 1/10th (2.5 mg.) the dosage level of cortisone and hydrocortisone and ½ less dosage level than prednisone or prednisolone.

on shortening the period of resolution which follows the attainment of maximal activity.[32] The duration of inflammatory activity in the prophylactically treated groups in most instances was about two weeks and no recurrence of ocular lesion was noted beyond this period.

EXPERIMENT 2

Comparative treatment of established uveitis lesions

The comparative anti-inflammatory effects of triamcinolone free alcohol, and other corticosteroids, when given 24 hours after the onset of established uveitis, were studied in this experiment. The techniques of Schlaegel and Davis,[38] cited by O'Rourke and associates,[32] were used in this experiment.

Again 18 full-grown albino rabbits with normal eyes were sensitized to 0.5 cc. undiluted horse serum (Lederle) by subcutaneous injection beneath the shaved abdominal skin at four separate areas. The subcutaneous injections were repeated every week for three weeks to produce maximal cutaneous sensitivity; in some animals an "Arthus phenomenon" with necrosis of abdominal skin was observed. At the end of 28 days, a shock dose of 0.1 cc. of the same antigen was injected intravitreously under sterile conditions and pentobarbital (Nembutal) anesthesia, using the same technique mentioned in Experiment 1. The onset of inflammatory lesions was rapid, within 24 hours with maximal response. All the five graded features were observed with slitlamp and ophthalmoscopic examination and were found to be much more prominent than those observed in Experiment 1 (figs. 2a, 2b, 3 and 4).

The same dosage schedule of corticosteroids, as indicated in Table 1, was used. Triamcinolone free alcohol was given at one-tenth the level of cortisone and hydrocortisone and one-half the level of prednisolone. The steroid injections were given 24 hours after development of uveitis lesions and were repeated every day for seven days. All the animals were examined each day with slitlamp and ophthalmoscopic observations were recorded according to the method previously mentioned.

Results. In control animal eyes, the inten-

sity and character of the graded inflammatory signs were much more severe and progressive during the first three to five days, to a maximal severity on the fifth day. Our observations and findings were apparently the same as those of previous investigators.[32] In all steroid-treated animal eyes the graded inflammatory activities were greatly reduced within three to four days (figs. 2b and 4). The suppressive effect of triamcinolone free alcohol treated groups was somewhat superior to the prednisolone treated group, and these were superior to the cortisone and hydrocortisone groups. The five features of uveitis were less severe in the triamcinolone free alcohol group than in the other groups.

During daily treatment for one week triamcinolone free alcohol, the greatest and most rapid suppressive effect on uveitis activity was seen by the seventh day (fig. 4). As can be seen, the anti-uveitis activity of cortisone, hydrocortisone and prednisolone was less but tended to be most marked by the seventh to ninth day. ACTH was relatively ineffective. The complete or partial suppression of uveitis activity by all corticosteroids tested, occurring between the seventh and ninth days, was similar to the findings in previous studies.[32]

Experiment 3

Estimation of quantitative triamcinolone free alcohol potency in uveitis

The estimation of triamcinolone free alcohol potency in the treatment of active experimental uveitis required studies at various dose levels. Fifteen full-grown albino rabbits with normal eyes were used for the induction of uveitis lesions of maximal severity according to the procedure mentioned in Experiment 2. The animals were divided into five groups of three animals, and each group was treated daily by intramuscular injections of triamcinolone free alcohol for a week according to the dosage schedules shown in Table 2. The observations of slitlamp and ophthalmoscopic examination were recorded each day for 15 days, as described in the previous studies.

Results. In the treated animals a marked suppression of uveitis activity was observed as compared to the control groups. Among the four groups treated with triamcinolone free alcohol, the dosage ranged from 0.5 to 3.5 mg./kg. of body weight; only minor differences in degree of uveitis activity were noted during a period of seven days of treatment. On the eight or ninth day of the experiment, the response was similar in all treated

TABLE 2

PLANS FOR DOSAGE SCHEDULE FOR QUANTITATIVE ESTIMATION OF TRIAMCINOLONE FREE ALCOHOL POTENCY LEVEL*

Group Number	Treatment	Daily Dose (intramuscular)	Human 70 kg. Equivalent Dosage and Potency Level	Remarks
1	Triamcinolone free alcohol	3.5 mg./kg.	245 mg.	Approximately ½ less dosage level than prednisone or prednisolone
2	Triamcinolone free alcohol	2.5 mg./kg.	175 mg.	½ less dosage level than prednisone or prednisolone
3	Triamcinolone free alcohol	1.0 mg./kg.	70 mg.	½ less dosage level than prednisone or prednisolone
4	Triamcinolone free alcohol	0.5 mg./kg.	35 mg.	1/10 less dosage level than prednisone or prednisolone
5	Placebo (normal saline)	1 cc./kg.	70 cc.	Control group

* Based upon several reductions of dosage level of Triamcinolone free alcohol (Aristocort, Lederle).

groups; the same type of response was noted in Experiment 2 during the period of seven to nine days.

The suppression of uveitis activity depends on adequate continuing doses of steroid therapy. Some reactivation was noted in the groups receiving less than one mg. of triamcinolone free alcohol per kilogram of body weight (fig. 5). However, such recurrences did not develop in those groups receiving 2.5 or 3.5 mg./kg. during the observation period of two weeks. Therefore, the necessity of an adequate maintenance dosage level according to the potency of the drug becomes evident. Similar reports dealing with cortisone, hydrocortisone, ACTH, and prednisone treated animals were noted by several authors.[7, 32, 47] However, with triamcinolone free alcohol no difference was observed over a range of 1.0 to 3.5 mg./kg. of body weight, despite the fact that in induced uveitis the treatment was withheld after seven days and the established lesions were 24 hours old.

Comment

Chemistry first isolated the adrenal corticosteroids, cortisone and hydrocortisone and next produced prednisone and prednisolone, synthetic drugs. More recently the steroid structure of triamcinolone free alcohol and its derivative triamcinolone acetonide has been modified in an attempt to decrease the undesirable effects and to enhance the glucocorticoid (anti-inflammatory) activity, and greatly diminished mineralocorticoid (electrolyte and water) activity. Triamcinolone acetonide was not available for parenteral administration and, therefore, the triamcinolone free alcohol preparation was used in these experiments in rabbits.

Side-effects do occur to some degree with all these corticosteroids; especially when a higher dose of the older steroids is used for long-term therapy is the incidence of side-effects greater. Experimentally, on weight basis levels in rabbits, no adverse effects were noticed even in those animals receiving the higher doses of triamcinolone and other corticosteroids used in this experiment for short-term therapy.

The suppression of uveitis activity depends upon the adequate maintenance dosage levels of triamcinolone free alcohol or other steroid therapy. However, the value of these agents is greater if they are administered early; the course of disease may show better response and recurrence may be prevented.

The excellent response of acute uveitis in experimental rabbits to triamcinolone free alcohol therapy may have something of therapeutic value for present clinical problems. Comparative animal studies of anti-inflammatory blocking effects, both in prophylaxis (moderate type) and in treating established acute uveitis (severe type), indicate that triamcinolone free alcohol has a potency equal to that of other steroids used in these experiments. Moreover, 10 to 20 times higher doses were required for cortisone and hydrocortisone, and two to five times higher doses required for prednisone and prednisolone; 60 mg./day of cortisone and hydrocortisone, or 20 to 40 mg./day of prednisone and prednisolone are needed to equal the effect of 10 to 20 mg./day of triamcinolone free alcohol. This dosage seemed adequate for the treatment of acute ocular inflammatory lesions in the human cases which will be reported in the clinical studies (Part II).

Summary and Conclusion

1. Comparative studies of anti-inflammatory blocking effects of various steroids in experimental rabbits with induced uveitis (moderate type) for prophylactic therapy, and for the treatment of established uveitis (severe type) lesions, demonstrated that triamcinolone free alcohol was as effective or more potent than older steroids.

2. Triamcinolone free alcohol was 10 to 20 times more active than cortisone and hydrocortisone and two to five times more active than prednisone and prednisolone.

3. No significant side-effects were observed in the experimental rabbits treated with triamcinolone free alcohol and other

corticosteroids giving the highest dosage levels (highest mg./kg. body weight) in continuing adequate doses for a short-term therapy of seven days.

4. No reactivation of inflammatory response was noticed in the acute established uveitis (severe type) groups receiving triamcinolone free alcohol in doses adequate for short-term therapy (1.0 to 3.5 mg./kg. body weight).

Georgetown University
Medical Center (7).

References

1. Abrahamson, I. A., Jr., and Abrahamson, I. A., Sr.: Metimyd: A clinical study. Am. J. Ophth., **42**: 482-485, 1956.

2. ———: Metreton: A clinical study. Am. J. Ophth., **45**:27-30, 1958.

3. Appel, B., Tye, M. J., and Leibsohn, E.: Triamcinolone in selected dermatoses. Antibiot. Med. & Clin. Therapy, **5**:716-719 (Dec.) 1958.

4. Bernstein, S.: The chemistry and biological activities of 16-hydroxylated steroids. In Recent Progress in Hormone Research. New York, Academic Press, 1958, v. 14.

5. Bernstein, S., Lenhard, R. H., Allen, W. S., Heller, M., Littell, R., Stolar, S. M., Feldman, L. I., and Blank, R. H.: 16-hydroxylated steroids: IV. The synthesis of the 16 alpha-hydroxy derivates of 9 alpha-halo-steroids. J. Am. Chem. Soc., **78**:5693, 1956.

6. Berntsen, C. A., Jr., Freyberg, R. H., Kammerer, W. H., and Hellman, L.: An early progress report on the effects of 16-alpha-hydroxy, delta 1,-9 alpha-fluorohydrocortisone (triamcinolone). Presented at the New York Rheumatism A., April, 1957.

7. Biegel, A. C.: Effects of cortisone on horse serum uveitis. Arch. Ophth., **45**:258 (Mar.) 1951.

8. Black, R. L., Yielding, K. L., and Bunim, J. J.: Observations on new synthetic antirheumatic steroids and critical evaluation of prednisone therapy in rheumatoid arthritis. J. Chron. Dis., **5**:751 (June) 1957.

9. Boland, W. W.: Experiences with 9-alpha-fluorohydrocortisone acetate in rheumatoid arthritis. Am. New York Acad. Sc., **61**:591 1955.

10. Demos, C. H.: Personal communication.

11. Diaz Tellechea, C. M.: Triamcinolone in the treatment of idiopathic thrombopenic purpura. Arch. Int. Med., **18**:2 (Mar.-Apr.) 1958.

12. Dubois, E. L.: Triamcinolone in the treatment of systemic lupus erythematosus. J.A.M.A., **167**: 1590-1599 (July) 1958.

13. ———: Evaluation of steroids in systemic lupus erythematosus with particular emphasis on triamcinolone and methylprednisolone. Metabolism, **7**:509-525 (July) 1958.

14. Duke-Elder, S.: Parson's Diseases of Eye. New York, Macmillan, 1954, ed. 12, pp. 124-125.

15. Epstein, J. I., and Sherwood, H.: The use of aristocort in diseases of allergy. Connecticut Med., **22**:822-823 (Dec.) 1958.

16. Feinberg, S. M., Feinberg, A. R., and Fisherman, E. W.: Triamcinolone (Aristocort): New corticosteroid hormone: Its use in treatment of allergic disease. J.A.M.A., **167**:58-59 (May) 1958.

17. Foss, B.: Experimental and anaphylactic iridocyclitis. Acta path. & microbiol., Scand. (Supp.) **81**: 3-128 (Sept.) 1949.

18. Freyberg, R. H., Berntsen, C. A., and Hellman, L.: Further experiences with 9-alpha-fluoro, 16-alpha-hydroxy-hydrocortisone (triamcinolone), in treatment of patients with rheumatoid arthritis. Presented at 9th Internat. Conf. Rheumatic Dis., Toronto, Canada, June 24, 1957.

19. Friedlaender, S., and Friedlaender, A. S.: Use of triamcinolone: A new corticosteroid in the management of allergic disease. Antibiot. Med. & Clin. Therapy, **5**:315-321 (May) 1958.

20. Gordon, D. M.: Prednisone and prednisolone in ocular disease. Am. J. Ophth., **41**:593-600 (Apr.) 1956.

21. Hartung, E. F.: The treatment of rheumatoid arthritis: Experiences with triamcinolone. J. Florida Acad. Gen. Pract., **8**:1825 (Jan.) 1958.

22. ———: Triamcinolone in treatment of rheumatoid arthritis. J.A.M.A., **167**:973-976 (June) 1958.

23. Hellman, L., Zumoff, G., Kretchmer, N., Minsky, A., and Kramer, B.: The treatment of the nephrotic syndrome with triamcinolone. A.M.A.J. Dis. Child., **94**:437 (Oct.) 1957.

24. Hellman, L., Zumoff, B., Schwartz, M. K., Gallagher, T. F., Berntsen, C. A., and Freyberg, R. H.: Antirheumatic and metabolic effects of a new synthetic steroid. Ann. Rheumat. Dis., **16**:141-144 (Mar.) 1957.

25. Hollander, J. L., Brown, E. M., Jessar, R. A., Smukler, N. M., Udell, L., Shanahan, J. R., Stevenson, C. R., and Bowie, M. A.: The effect of triamcinolone on psoriatic arthritis. Arthritis & Rheumat., **1**:285-287 (June) 1958.

26. Kalz, F.: The effects of triamcinolone (Aristocort) and 6-methylprednisolone on some skin diseases. Canad. M. A. J., **79**:400-401 (Sept.) 1958.

27. Kanee, B.: The use of triamcinolone (Aristocort) in selected dermatoses. Canad. M.A.J., **79**:748-751 (Nov.) 1958.

28. King, J. H., Jr., and Weimer, J.: Prednisone and prednisolone in ophthalmology: Experimental and clinical studies. Arch. Ophth., **54**:46-54, 1955.
29. Lepri, G.: Studies on cortisone in ophthalmology. Am. J. Ophth., **35**:935-946 (July) 1952.
30. McGavack, T. H.: Clinical experiences with triamcinolone in elderly men. Am. J. M. Sc., **236**:720-734 (Dec.) 1958.
31. Mullins, J. F., and Wilson, C. J.: Triamcinolone diacetate (Aristocort) in the treatment of varied dermatoses. Texas J. Med., **54**:648-650 (Sept.) 1958.
32. O'Rourke, J. F., Iser, G., and Ryan, R. W.: An initial evaluation of prednisone therapy in ocular inflammation. Arch. Ophth., **55**:323-332 (Mar.) 1956.
33. Pariser, H.: The use of triamcinolone (Aristocort) in dermatology. Virginia M. Month., **85**:673-675 (Dec.) 1958.
34. Perrine, J., Bell, P., Bortle, L., Heyder, E., Ross, E., and Ringler, I.: The biological activity of triamcinolone and related steroids. J. Pharmacol. & Exper. Therap., **122**:60A (June) 1958.
35. Rein, C. R., Fleischmajer, R., and Rosenthal, A. L.: Use of a new corticosteroid (Aristocort diacetate) in dermatology. J.A.M.A., **165**:1821-1823 (Dec.) 1957.
36. Robinson, R. C. V.: Treatment of dermatoses with local application of triamcinolone acetonide: A new synthetic corticoid. Univ. Maryland M. Bull., **43**:54-57, 1958.
37. Rome, S., et al.: ACTH and cortisone in ocular inflammations: Parenteral and local use. Ann. West. Med. & Surg., **4**:799-804, 1950.
38. Schlaegel, T. F., Jr., and Davis, J.: Reaction of rabbit eye to normal horse serum. Am. J. Ophth., **26**:785 (Aug.) 1943.
39. Schwartz, E., and Levin, L.: Triamcinolone therapy in chronic intractable bronchial asthma. A.M.A. Conv., San Francisco, June, 1958.
40. Segal, M. S., and Duvenci, J.: Aristocort therapy in bronchial asthma. Tufts N.E. Medical Center, **4**:71-79 (April-June) 1958.
41. Shelley, W. B., Harun, J. S., and Pillsbury, D. M.: The treatment of psoriasis and other dermatoses with triamcinolone (Aristocort®). J.A.M.A., **167**:959-964 (June) 1958.
42. Sherwood, H., and Cooke, R. A.: A preliminary evaluation of a new corticosteroid in allergic diseases. J. Allergy, **28**:97 (Mar.) 1957.
43. Smith, J. G., Jr., Zawisza, R. J., and Blank, H.: Triamcinolone acetonide. A highly effective new topical steroid. Arch. Dermat., **78**:643-645 (Nov.) 1958.
44. Spain, D. M., and Molomut, N.: Effects of cortisone on development of tuberculosis lesions in guinea pigs and on their modification by streptomycin therapy. Am. Rev. Tuberc., **62**:337-344 1950.
45. Spies, T. D.: The influence of nutritional processes on aging. South. M. J., **50**:216-255 (Feb.) 1957.
46. Vogel, A., and Leopold, I. H.: Effect of compound F on horse serum uveitis in the rabbit eye. Am. J. Ophth., **36**:690 (May) 1953.
47. Woods, A. C.: Clinical and experimental observation on use of ACTH and cortisone in experimental ocular inflammatory diseases. Am. J. Ophth., **33**:1325-1348, 1950; Tr. Am. Ophth. Soc., **48**:281, 1950.
48. Younger, D.; DiPillo, F., and McGinn, T.: Corticosteroid therapy in the treatment of erythema solare (sunburn). New York J. Med., **58**:2963-2964 (Sept.) 1958.
49. Zuckner, J.; Ramsey, R. H.; Caciolo, C., and Gantner, G. E., Jr.: Triamcinolone therapy in rheumatoid arthritis. Ann. Rheumat. Dis., **17**:398-405 (Dec.) 1958.

THE EFFECT OF ALPHA CHYMOTRYPSIN ON SUTURE MATERIALS*

S. M. Drance, M.D., R. G. Murray, M.D., and T. R. Smith, P.Eng.
Saskatoon, Canada

In 1958 Barraquer[1] published his report on the use of alpha chymotrypsin as a specific zonulytic agent in cataract surgery. His observations were based on animal experiments and human investigations. Considerable interest was aroused by his discovery and further reports by Cogan,[2] Ainslie,[3] Zorab,[4] and Rizzuti[5] have appeared.

Early in 1958 the enzyme was used in a group of unselected extractions in order to become familiar with the new technique, its indications, complications and long-term effects.[6] During the early part of the series it became apparent that the incidence of iris prolapse was very high. The main difference between our technique and Barraquer's was in the suture material used. He used silk while we used plain catgut. It was decided to change to chromic catgut or silk and to test

* From the Department of Ophthalmology and the Department of Mechanical Engineering, University of Saskatchewan.

the effects of the enzyme on the commonly used suture materials in vitro.

Experiment

Plain catgut (6-0) chromic catgut, and silk† were incubated in 1:5,000 alpha chymotrypsin† for one to 96 hours at 37°C. Normal saline control incubations were carried out. The tensile strengths of the suture materials were then tested and compared with non-incubated suture materials.

Method

Tests of many kinds have been used as measures of quality and uniformity of materials. The test to destruction in axial tension is a well-known standard method of evaluation of mechanical strength under conditions simulating actual service.

The functional requirements of a tensile testing machine are: (1) a means of applying load or force, (2) a means of measuring the load, and (3) a means of measuring dimensional change in the specimen. The latter function was not deemed necessary for the tests described here, and in any event is usually met by auxiliary equipment.

The loading of the specimen is done manually in the device shown in Figure 1. A knurl-headed screw, rotated by the fingers, is connected to a simple linkage exerting a downward pull on the specimen. The specimen is suspended as a single strand from a small chain attached to a thin metal ribbon wrapped around a cylindric cam. This cam exerts a torque balanced and indicated by a simple pendulum. This pendulum arrangement is the weighing mechanism. Calibration of the visual scale was obtained by suspending metric weights on the chain. Such a system is inherent in most commercial weigh scales, being simple, rugged, and reliable.

Specific requirements of the testing device were determined through some preliminary tests in which an attempt was made to measure the approximate range of strengths and to devise a method of gripping the specimens. These tests were conducted by syphoning water into a small container hung from a strand of gut. The rupture strength was obtained by weighing the vessel and contents, after the gut had separated. The information gained in this way suggested the range of load and dimensions of the device used.

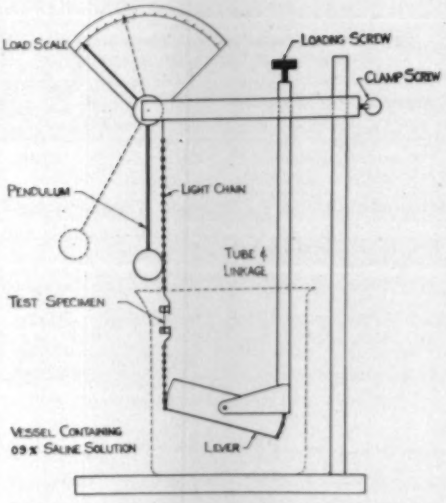


Fig. 1 (Drance, Murray and Smith). Tension testing device for surgical gut.

One important secondary functional requirement of the tension testing apparatus is the method of grasping the material. Knotting, wedging or clamping were rejected. Wrapping the gut around the cylindrical surface of 5/16 inch diameter plastic tubing proved to be satisfactory. In this way sharp kinks or pinching were avoided, the tensile load being developed gradually by friction. The free end was secured by wedging it into the terminal anchoring.

In general the length of the specimen has no bearing on the tensile strength. An attempt was made to get at least eight or more tests to exclude accidental errors, such as might occur through kinking in handling.

All tests were conducted at room temperature (about 75°F.) with the specimens immersed in a bath of normal saline solution.

† All suture materials were made by the Ethicon Company and generously supplied by the University Hospital, Saskatoon. Alpha chymotrypsin was generously supplied by British Drug Houses, Ltd.

TABLE 1

THE TENSILE STRENGTH OF SUTURE MATERIALS INCUBATED IN ALPHA CHYMOTRYPSIN

Mean Tensile Strengths (in gm.)	Plain Catgut	Chromic Catgut	Silk
Nonincubated suture	209	255	238
Saline-incubated suture for 96 hr.	176	229	238
Enzyme-incubated suture for 1 hr.	210	—	—
10 hr.	191	228	—
20 hr.	—	230	—
32 hr.	144*	206*	247
56 hr.	136*	218*	207
96 hr.	93*	197*	236

* Significant at the one-percent level.

Specimens were submitted in sealed or capped containers identified by code unknown to the individual operating the testing device.

RESULTS

Table 1, Column 1 shows the mean tensile strengths of the plain catgut in gm. The results were analyzed by the multiple range and multiple F tests[7] at the one-percent point (p less than 0.01) indicate that the saline-incubated catgut shows no significant change in tensile strength even after 96 hours, whereas, the enzyme-incubated catgut shows a significant decrease in tensile strength after 32 hours' incubation. It is to be noted that after 32 hours' incubation in enzyme the catgut was very friable on ordinary handling while the longest saline-incubated catgut could not be distinguished from the original material.

Table 1, Column 2 shows the average tensile strength of chromic catgut in gm. The analyzed results show that enzyme incubation produces a statistically significant fall in tensile strength after 32 hours' incubation while saline incubation after 96 hours produces no statistically significant change. The decrease in tensile strength of chromic gut is very much less marked than the decrease in strength of the plain catgut.

Table 1, Column 3 shows the average tensile strength of silk in gm. The values analyzed statistically show that there is no significant decrease in tensile strength between the original silk and both the saline and enzyme incubated samples.

DISCUSSION

The experiments in vitro leave little room for doubt that alpha chymotrypsin reduced the tensile strength of plain catgut. The effect on chromic catgut was much less marked, while no effect on silk was demonstrated.

Enzymatic action in general is very rapid and it can be supposed that the catgut is affected early during exposure to the enzyme. It may well be that in vivo with other enzymes and cellular materials present it requires little contact with the enzyme to weaken the catgut and allow the wounds to leak. There are many surgeons who are using plain catgut for wound closure in cataract surgery and the present paper is intended to show that alpha chymotrypsin may have adverse effect on some suture materials.

SUMMARY

A method for testing tensile strength of catgut, chromic catgut and silk is described.

In vitro effects of alpha chymotrypsin on tensile strength of catgut, chromic catgut and silk are described. Plain catgut is markedly weakened by the enzyme, chromic catgut shows a slight change, whereas, silk shows no change in tensile strength.

University of Saskatchewan.

REFERENCES

1. Barraquer, J.: Communication a la real academic de medicine de Barceloma. April 8, 1958.
2. Symonds, H. M., Cogan, T. E. H., and Gibbs, D. C.: Intracapsular extraction using alpha chymotrypsin. Brit. J. Ophth., **43**:193, 1959.
3. Ainslie, D.: Cataract extraction with the aid of alpha chymotrypsin. Brit. J. Ophth., **43**:200, 1959.
4. Zorab, E. C.: Alpha chymotrypsin in cataract surgery. Brit. J. Ophth., **43**:202, 1959.
5. Rizzuti, A. B.: Alpha chymotrypsin in cataract surgery. Arch. Ophth., **61**:135, 1959.
6. Murray, R. G., and Drance, S. M.: Tr. Canadian Ophth. Soc., to be published.

HISTOLOGY OF ZONULOLYSIS WITH ALPHA CHYMOTRYPSIN EMPLOYING LIGHT AND ELECTRON MICROSCOPY*

ALBERT P. LEY, M.D., ÅKE S. HOLMBERG,† M.D., AND TSUYOSHI YAMASHITA, M.D.
Saint Louis, Missouri

In April, 1958, Barraquer[1] reported a series of cataract extractions facilitated by enzymatic zonulolysis with alpha chymotrypsin. With the dilutions used in his experiments he noted no apparent effect on the lens and remainder of the intraocular structures. He concluded that the action of alpha chymotrypsin was selective for the zonule. This exciting discovery opens new avenues of exploration.

The purpose of these experiments is to demonstrate what microscopic alterations are produced in the crystalline lens and its supporting structures by the application of alpha chymotrypsin.

EXPERIMENTS

Thirty rhesus monkey eyes and 14 enucleated human eyes obtained from autopsies were used for these experiments. The monkeys ranged in weight from 3.0 to 5.5 kg. The animals had not been raised in captivity, hence the exact ages were not known; some appeared to be very old and a few young. The autopsy eyes were from persons 25 to 65 years of age. Fellow eyes were used as controls whenever indicated. The alpha chymotrysin‡ was employed in dilutions of 1:5,000 and 1:10,000.

Sections of paraffin- or celloidin-embedded formalin-fixed tissues were stained with hematoxylin and eosin, Alcian blue, and periodic acid Schiff stains for examination by light microscopy.

Representative samples of lens, zonule and ciliary epithelium were sectioned for electron microscopy after fixation in osmic acid and embedding in methacrylate.

I. IN VITRO

A. DEMONSTRATION OF THE EFFECT OF ALPHA CHYMOTRYPSIN INSTILLED INTO THE POSTERIOR CHAMBER

Approximately 0.2 cc. of alpha chymotrypsin was injected into the posterior chamber by inserting a 26-gauge hypodermic needle through the cornea across the anterior chamber, through the pupil and under the iris. Effort was made to distribute the enzyme evenly by sweeping the needle from side to side. The posterior chamber area immediately beneath the corneal perforation could not be reached through this anterior approach, and most preparations show intact zonules in this region. Control eyes were similarly injected with sterile saline solution. The eyes were then incubated at 37°C. for periods of time from five minutes to one hour. The eyes were fixed in 10 percent formalin. Whole mounts of lens-zonule preparations were made after fixation and stained with periodic acid Schiff reagent. Ten human eyes and eight monkey eyes were used for this group of experiments.

The stained lens-zonule mounts of alpha chymotrypsin treated eyes all show zonules in various stages of distintegration in direct relation to time of exposure to the enzyme (figs. 1, 2, and 3). In addition all show some increase in the diameter of the ciliary ring (fig. 4).

* From the Departments of Anatomy and Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine. This investigation was supported in part by a grant, B-1375, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service, Bethesda, Maryland.

† Fight-for-Sight Fellow of the National Council To Combat Blindness.

‡ Alpha chymotrypsin was obtained from two sources: Quimotrase from P.E.V. YA. Laboratories in Barcelona and Alpha Chymar from Armour Pharmaceutical Laboratories in Chicago. No differences were observed in the action of these two preparations.

In all these preparations the anterior vitreous face remains intact even after complete disruption of the zonules. Furthermore, in two of the younger human eyes and in all of the monkey eyes the anterior vitreous face appears to be firmly attached to the posterior lens capsule.

B. Demonstration of process of zonulolysis

In order to observe the process of zonulolysis lens-zonule-ciliary body preparations were made in the following manner:

First, a Flieringa ring was sutured to the sclera over the ciliary body; then the entire cornea was excised; next the anterior segment was removed by an incision at the equator; and last, the iris was torn from its insertion. This lens-zonule mount was placed in a Petri dish on the stage of a microscope and then bathed in alpha chymotrypsin. The disintegrating zonules were observed under 60-times magnification.

Within 10 to 15 minutes the zonules began to show, first, elongation and thinning, and then rupture. Progression to complete lysis of the zonules occurred in approximately 30 minutes. Despite continued bathing of the mount with enzyme for an additional 30 minutes, the anterior vitreous face remained intact. This enzymatic lysis of the zonules could be hastened by warming the alpha chymotrypsin solution.

At intervals of 5, 10, 15 and 60 minutes the process of disintegration was arrested by the addition of either 10-percent formalin or osmic acid in preparation for microscopic sections. Four human eyes and three monkey eyes were prepared in this manner. Untreated controls were similarly mounted for comparison.

Electron micrographs of the normal human and monkey controls show the zonules to be composed of very densely packed uniform fibrils of approximately 60 to 70 Ångström in thickness (figs. 5 and 6). These fibrils all appear to be oriented longitudinally and separated by less osmophilic ground substance. No banding or periodicity can be demonstrated in the fibrils seen in these sections. A pericapsular membrane of similar fibrillar structure is seen on the lens at the equator, but this is not observed in the central portion of either the anterior or posterior capsule. Marked variations in thickness of the lens capsule are shown in these electron micrographs of normal untreated eyes.

Sections of the treated eyes show disintegration of the long zonular fibrils into clusters of fragments of relatively uniform length of approximately 1000 Å. (figs. 7, 8, 9, and 10). Some sections of the lens near the equator show similar fragmentation of the pericapsular membrane but these changes are confined to the surface of the capsule. The capsule proper shows no alteration even in the finer details of its structure (fig. 11). The treated eyes also show gross variations in thickness of the capsule. In some sections the capsule of the control eye appears much thinner than in the enzyme-treated eye; while in contrast, other eyes show the reverse.

No alterations can be observed in the internal limiting membrane of treated human or monkey eyes (figs. 12 and 13). The ciliary epithelium of treated monkey eyes appears normal. Human eyes, both treated and controls, show only the expected postmortem changes in the ciliary epithelium commonly seen in autopsied material. The internal limiting membrane, zonules and capsule are notably resistant to postmortem autolysis.

II. In vivo

A. Demonstrations of effects of enzyme under surgical conditions

Five monkeys, under short-acting barbiturate (Surital) anesthesia, supplemented with retrobulbar lidocaine injection, were subjected to lens extraction from the right eye. Left eyes were used for control. An effort was made to simulate as nearly as possible actual aseptic operating conditions. Alpha chymotrypsin 1:5,000 was used to irrigate the posterior chamber after the keratome

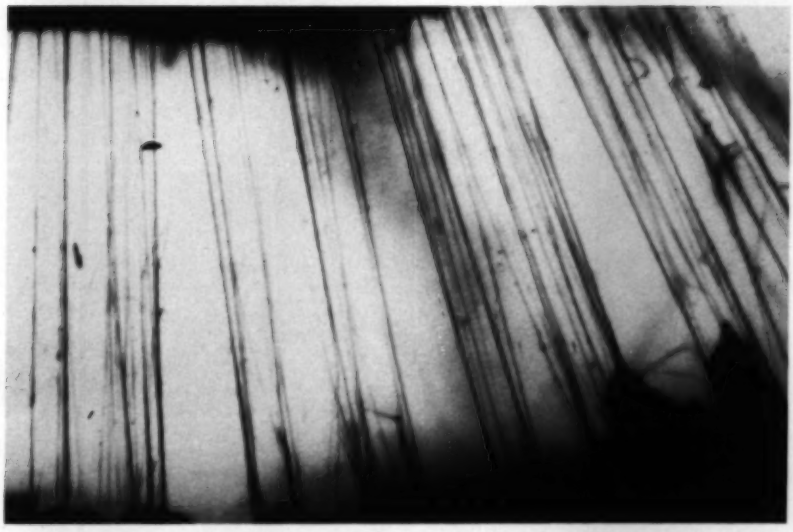


Fig. 1 (Ley, Holmberg and Yamashita). Zonulolysis in human eye arrested at stage of thinning and stretching of zonules. (0.2 cc. 1:10,000 alpha chymotrypsin into posterior chamber in vitro, ×60.)

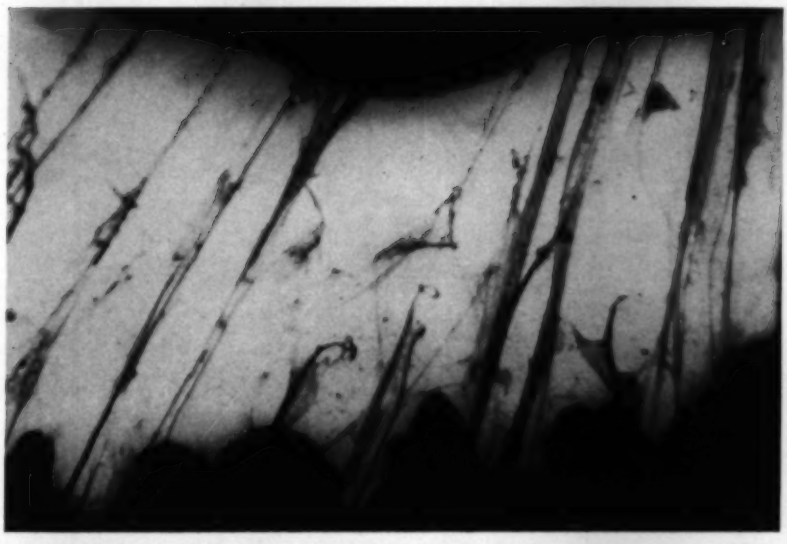


Fig. 2 (Ley, Holmberg and Yamashita). Zonulolysis in human eye arrested at stage of beginning fragmentation of zonules (0.2 cc. 1:10,000 alpha chymotrypsin into posterior chamber in vitro). Note that the zonules are not separating from the capsular attachment, but are thinning and fragmenting in more or less random fashion. (×60.)

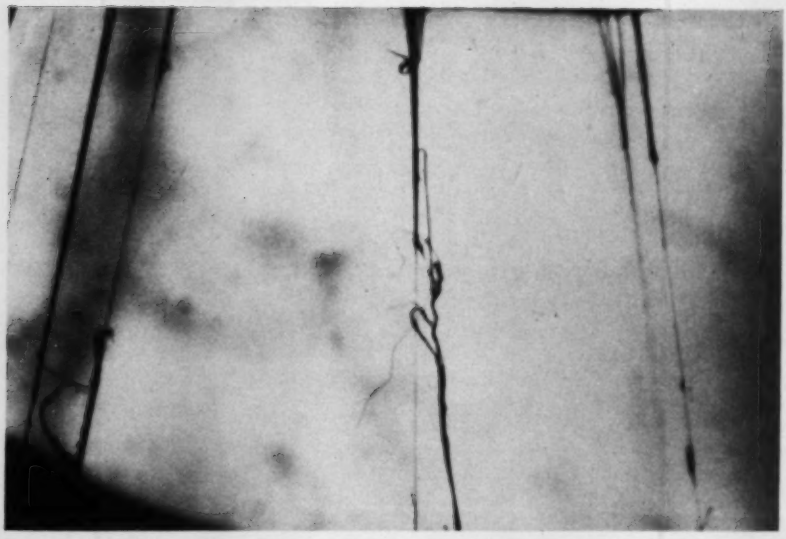


Fig. 3 (Ley, Holmberg and Yamashita). Zonulolysis in human eye arrested at stage of almost complete disintegration of the zonules. (0.2 cc. alpha chymotrypsin into posterior chamber in vitro). Note that most of the remaining few zonules are thinner in the central portion and are thicker adjacent to the lens capsule above and the ciliary body below. (×60.)

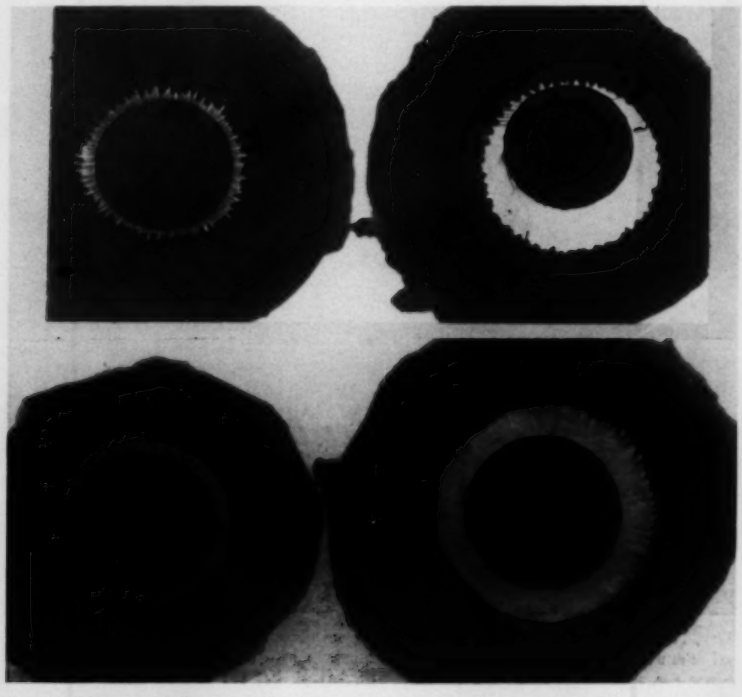


Fig. 4 (Ley, Holmberg and Yamashita). Comparison of pairs of whole mounts of lens-zonule preparations in human eyes (above) in vitro, and monkey eyes (below) in vivo. Both right eyes were treated with 1:5,000 alpha chymotrypsin, 0.2 cc. injected into posterior chamber. Note the diameter of ciliary ring is greater in each treated eye, although the monkey eye is only 15 minutes after treatment and the zonules are stretched but unbroken.

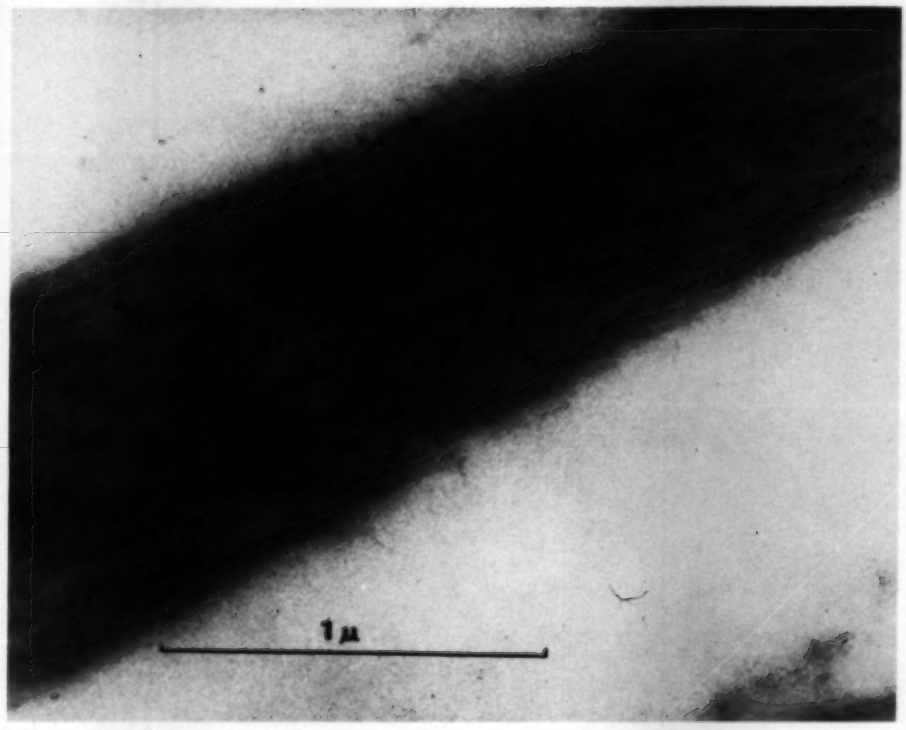


Fig. 5 (Ley, Holmberg and Yamashita). Electron micrograph of a longitudinal section through a portion of a single normal human zonule showing the multiplicity of regularly oriented fine fibrils which make up the basis of its structure. (×60,000.)

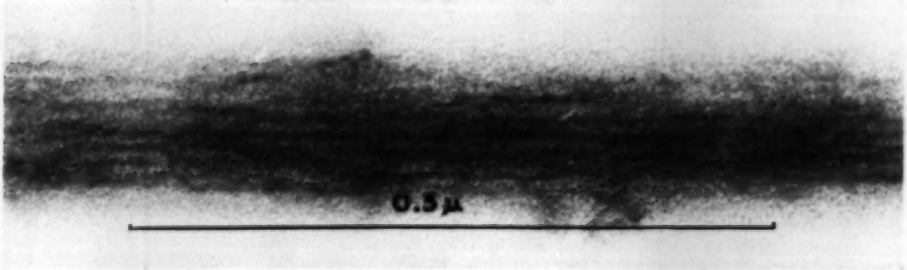
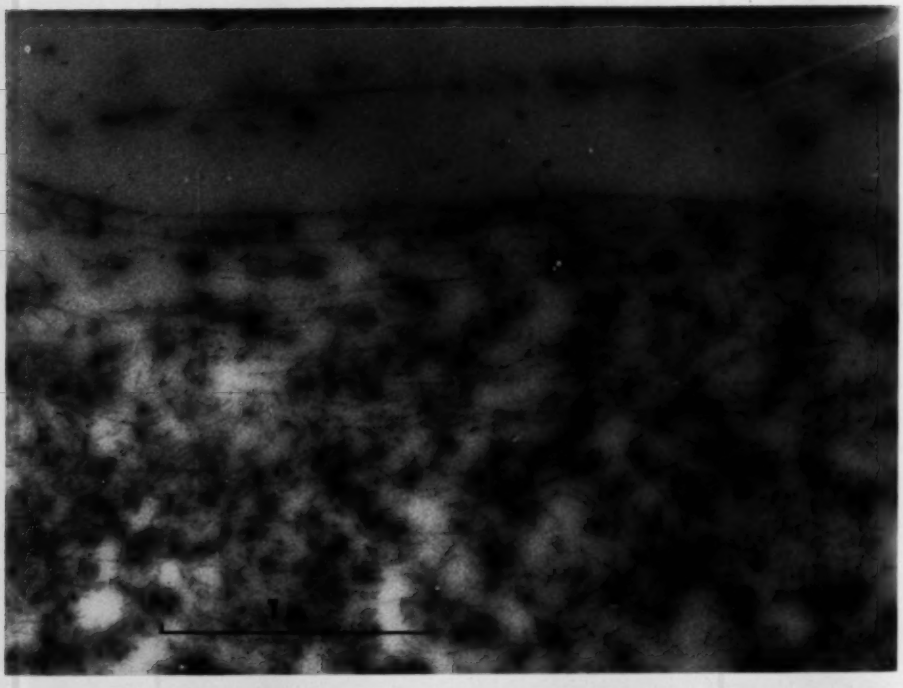


Fig. 6 (Ley, Holmberg and Yamashita). Higher resolution of section of zonule shown in Figure 5. This further demonstrates the uniformity of the fibrils and their lack of any obvious periodicity. (×160,000.)



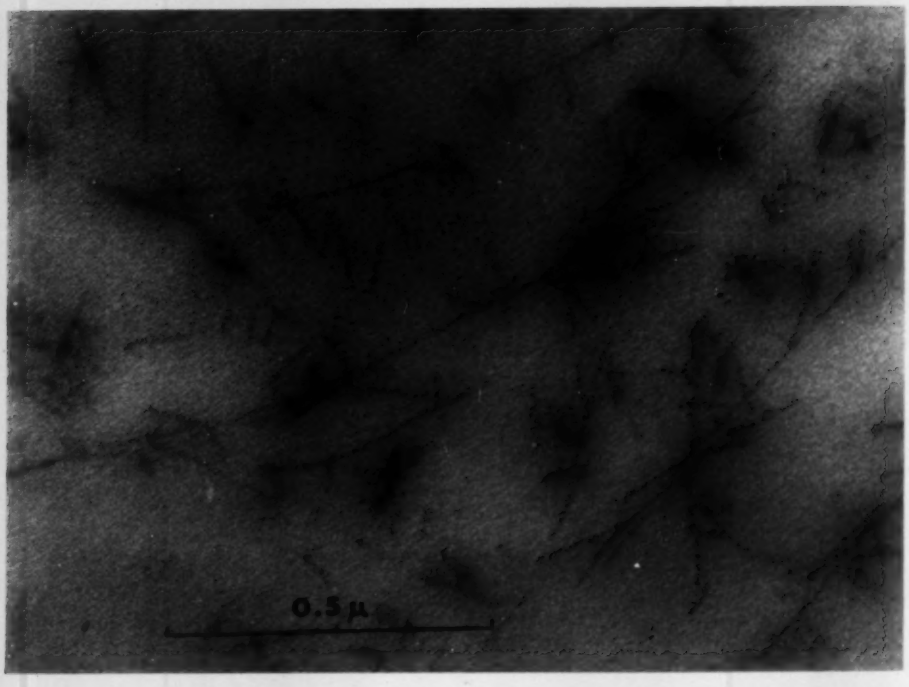

0.5 μ

Fig. 7 (Ley, Holmberg and Yamashita). Electron micrograph of a portion of human zonule 10 minutes after treatment with 1:5,000 alpha chymotrypsin. Most of the fine fibrils show disintegration into clusters of fragments of relatively uniform length. Some fibrils still appear intact. (×42,000.)

Fig. 9 (Ley, Holmberg and Yamashita). Electron micrograph of an area of a single monkey zonule 15 minutes after treatment with 1:5,000 alpha chymotrypsin, showing beginning of fragmentation of fibrils. (×60,000.)

Fig. 8 (Ley, Holmberg and Yamashita). Electron micrograph at high resolution of an area of a single human zonule five minutes after treatment with 1:5,000 alpha chymotrypsin, showing the regularity of the fragmentation of the fibrils. (×100,000.)

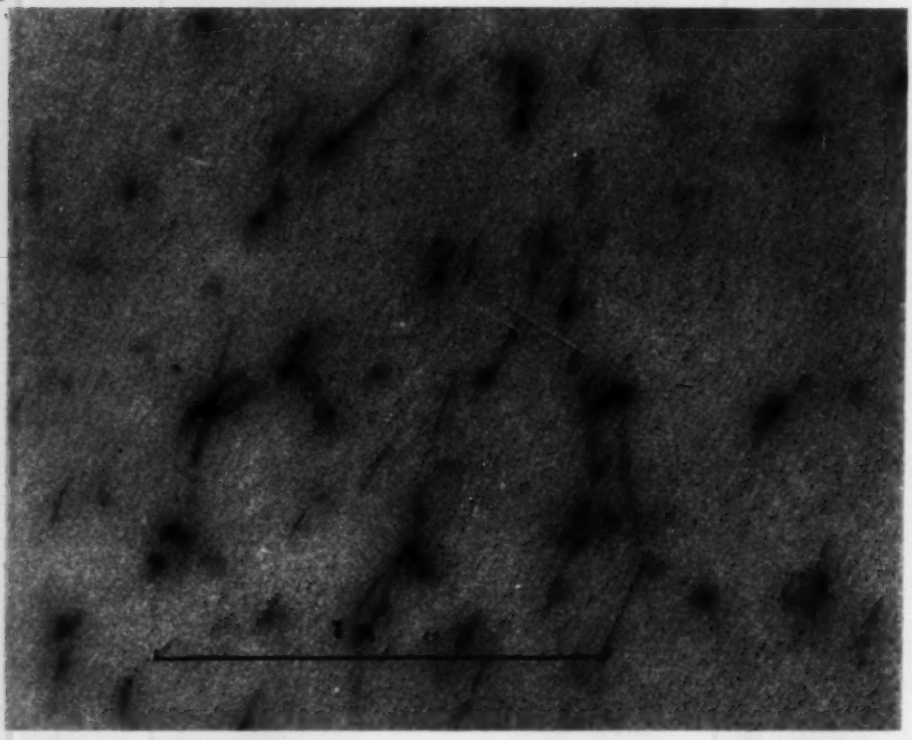


Fig. 10 (Ley, Holmberg and Yamashita). Electron micrograph of an area of a monkey zonule one hour after treatment with 1:5,000 alpha chymotrypsin, showing complete fragmentation of fibrils. (×70,000.)

section was made. In four of the five animals intracapsular extraction of the lens was accomplished. In the fifth one, which appeared to be a very young animal, repeated irrigation of the posterior chamber with 1:5,000 alpha chymotrypsin did not weaken the zonules enough to permit intracapsular extraction. Three preplaced virgin silk sutures were used to approximate the wounds. The animals were killed at one, two and six-week intervals after the operation. The eyes were promptly fixed in 10 percent formalin after representative sections were cut for fixation in osmic acid.

In the four intracapsular extractions the lens appeared to bulge far forward within three to five minutes after instillation of the enzyme. In one animal Diamox was given intravenously immediately prior to lens extraction in an effort to forestall this complication, but the forward protrusion of the lens and vitreous did not seem lessened by this maneuver. The lenses could be removed easily with the erisophake, but in each case the vitreous could not be separated from its attachment to the posterior capsule. The postoperative course was benign in the operated eyes. The media remained clear so the fundus details were clearly visible at time of enucleation. No gross lesions could be detected either at time of enucleation or when the eyes were cut.

Microscopic sections showed no alterations of internal limiting membrane, ciliary epithelium, or retina in any of the postoperative specimens.

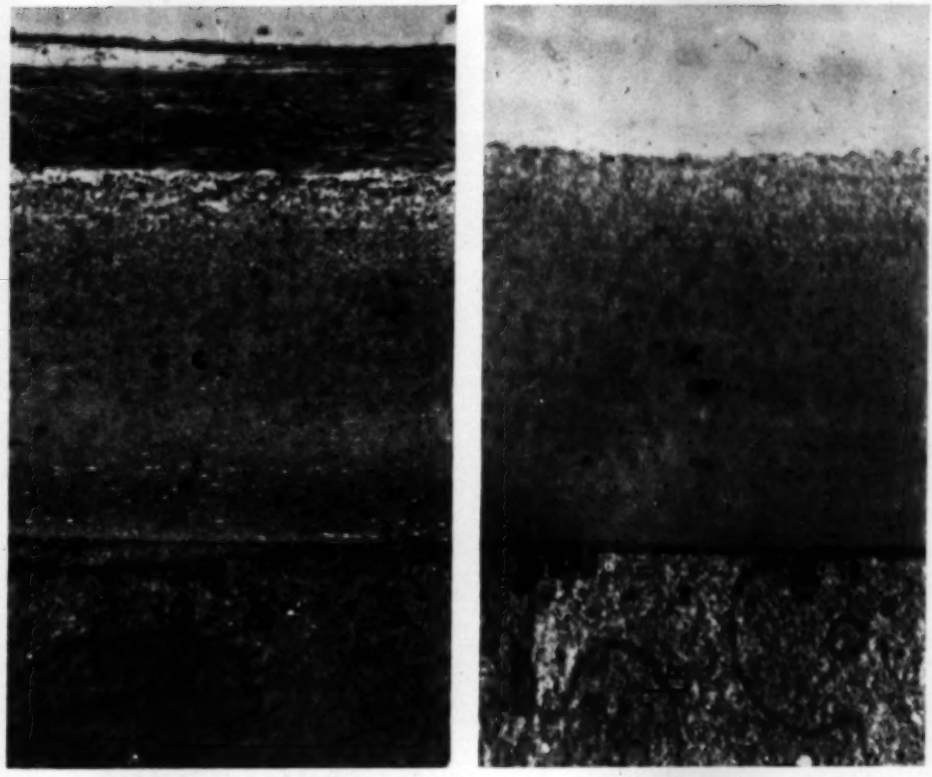


Fig. 11 (Ley, Holmberg and Yamashita). Electron micrograph of sections of human lens capsules at the equator. Left shows untreated and right shows comparable area five minutes after 1:5,000 alpha chymotrypsin. Z = zonule showing its composite fibrils. C = lens capsule. E = lens epithelium. (×7,000.)

B. Demonstration of effect of enzyme injected into posterior chamber

With same technique as outlined in Section I-A, above, alpha chymotrypsin was injected into the posterior chamber of anesthetized monkeys. Sterile saline was injected into the control eyes. Within three to five minutes following the injections, iridodonesis was observed in the enzyme-treated eyes. The animals were killed at 15 minutes, 1, 2, 3, 5, and 7 hours after injection. The eyes were fixed in 10-percent formalin, after representative sections were cut for fixation in osmic acid. Ten monkey eyes were used for this group of experiments.

All the eyes show marked dilatation of the ciliary ring, even to a considerable degree in the eye treated for only 15 minutes prior to enucleation (fig. 4-B). This eye shows only stretching of the zonules while all others show complete lysis. All the eyes demonstrate persistence of the ligamentum hyaloideo-capsulare, in two eyes even seven hours after injection of the enzyme (fig. 14). No microscopic changes can be seen in the ciliary epithelium in stained sections of the enzyme-treated eyes. The lens capsules of the enzyme-treated eyes appear to be of comparable thickness to those of the control eyes. The internal limiting membrane and the ciliary epithelium do not show any alterations in appearance by electron micros-

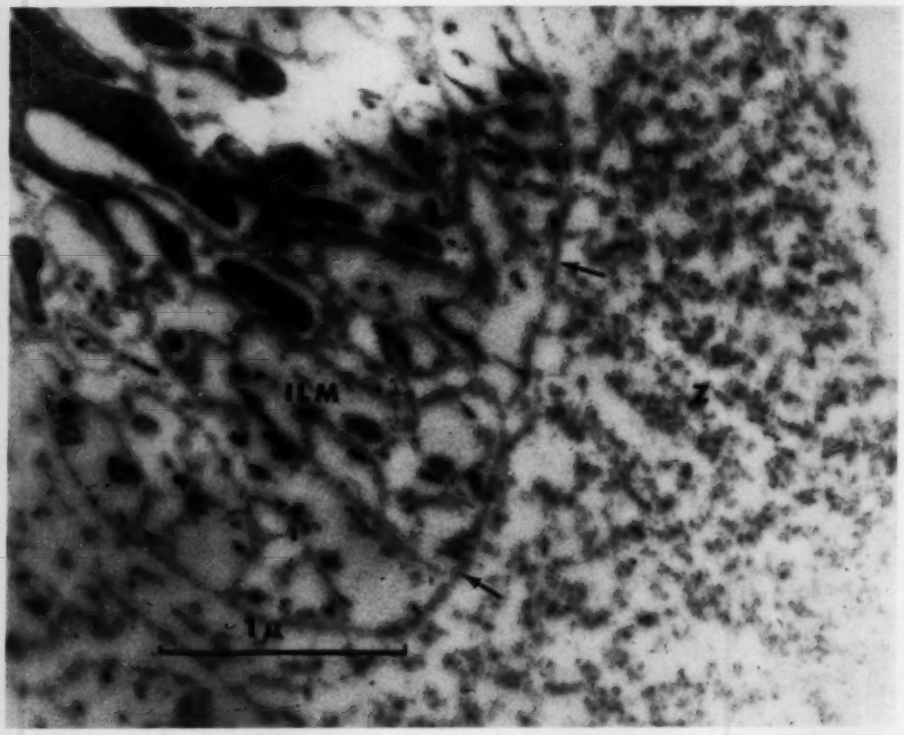


Fig. 12A (Ley, Holmberg and Yamashita). Electron micrograph of the apical area of human non-pigmented ciliary epithelium 10 minutes after treatment with 1:5,000 alpha chymotrypsin. ILM = internal limiting membrane which appears intact (arrows point to surface of internal limiting membrane). Z = fragmented zonular fibrils. (×38,000.)

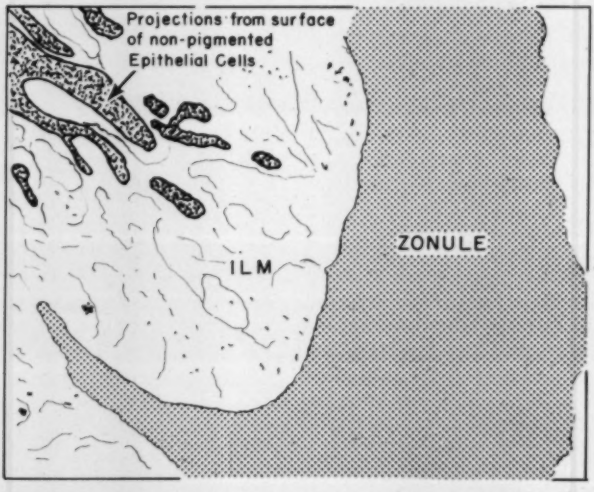


Fig. 12B (Ley, Holmberg and Yamashita). Schematic drawing of Figure 12A.

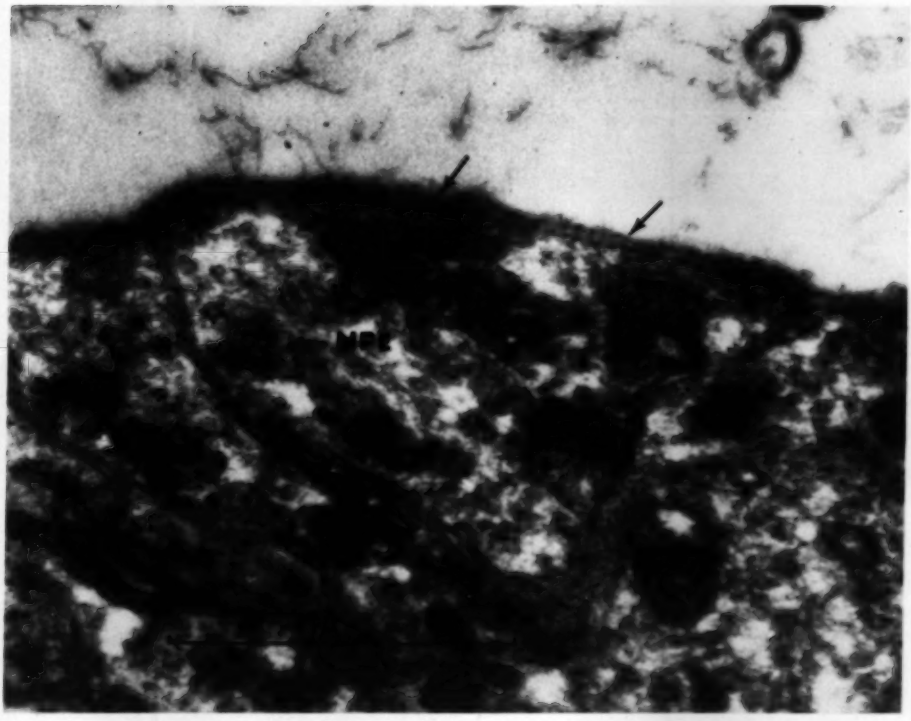


Fig. 13A (Ley, Holmberg and Yamashita). Electron micrograph of the apical area of monkey nonpigmented ciliary epithelium (NPE) one hour after treatment with 1:5,000 alpha chymotrypsin. The internal limiting membrane (arrows) is intact. Some fragmented zonular fibrils show above the internal limiting membrane. (×54,000.)

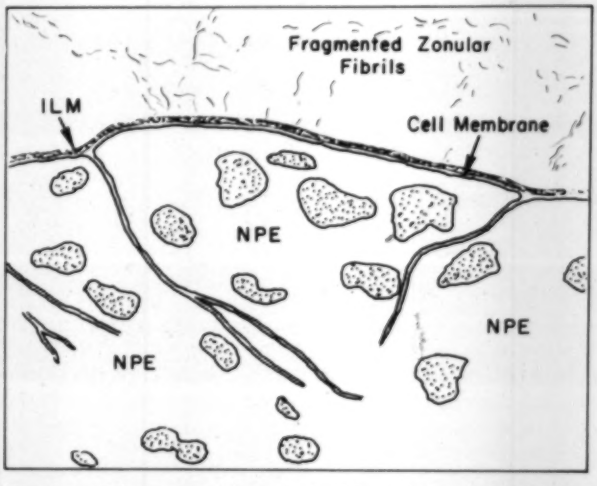


Fig. 13B (Ley, Holmberg and Yamashita). Schematic drawing of Figure 13A.

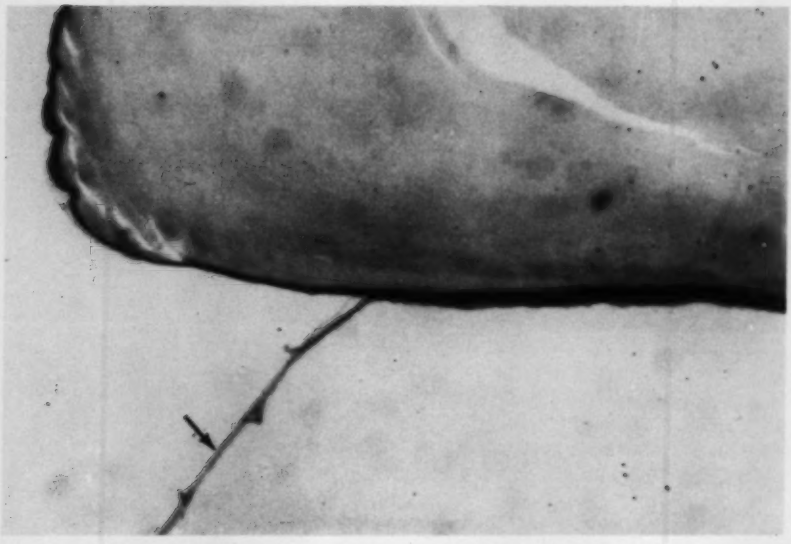


Fig. 14 (Ley, Holmberg and Yamashita). Section of alpha chymotrypsin-treated monkey eye stained with PAS and Alcian blue showing persistence of the ligamentum hyaloideocapsulare. Arrow points to blue staining vitreous face which joins the darker magenta staining capsule above. (×60.)

copy after 15 minutes and after one hour of exposure to 1:5,000 alpha chymotrypsin.

Discussion

I. Zonules

In all of these experiments a prompt lysis of the zonules was effected by alpha chymotrypsin in dilutions of 1:5,000 and 1:10,000 with but one exception. The only failure of the enzyme to produce zonulysis occurred under operating conditions of attempted lens extraction in a younger monkey; 1:5,000 dilution was being used in this instance. No striking differences were noted in the effect of the 1:5,000 dilution over that of 1:10,000.

Rupture of the zonules appears to be preceded by thinning and stretching of the zonules and dilatation of the ciliary ring. The stretching or dilatation of the ciliary ring was observed both in human eyes in vitro and in monkey eyes in vivo. This widening of the ciliary opening may account for the marked forward bulging of lens and vitreous that was noted during the operations for lens extraction. The forward displacement of lens and vitreous occurs within three to five minutes after injection, and 10 to 15 minutes before actual rupture of any zonules can be observed. Retrobulbar akinesia and intravenous Diamox did not prevent this forward protrusion of the lens and vitreous.

The pattern of fragmentation of zonular fibrils as seen in the electron micrographs has a uniformity which suggests that the protein of these fibrils has a regularly occurring amino-acid linkage which is subject to attack by the endopeptidase, alpha chymotrypsin. This invites further study of the details of the composition of the zonules.

II. Anterior vitreous face

In all of the experiments it can be shown that alpha chymotrypsin in the dilutions used has no appreciable effect on the anterior hyaloid face. Moreover, the exposure of the eye to this enzyme, even when prolonged far beyond the time required to effect complete disintegration of the zonules, does not lyse the attachment of the lens to the anterior

vitreous face. The ligamentum hyaloideocapsulare persisted in all of the monkey eyes and the younger human eyes treated with alpha chymotrypsin.

III. Internal limiting membrane and ciliary epithelium

The internal limiting membrane over the nonpigmented epithelium of the ciliary body in the human is a relatively large structure of variable thickness between 0.5 to 4.0μ as compared with the monkey in which this is a small structure of rather uniform thickness, 0.03 to 0.4μ (Holmberg[3, 4]). Nevertheless, alpha chymotrypsin in dilutions of 1:5,000 and 1:10,000 does not produce any demonstrable changes in these membranes covering the ciliary epithelium in either monkey or human eyes.

The monkey nonpigmented ciliary epithelium itself does not show any alterations after enzymatic zonulolysis has been effected by the alpha chymotrypsin. Because of the postmortem changes already present in human autopsy eyes, no evaluation can be made of the changes seen in human epithelium. This is in contrast to the zonules, lens capsule and internal limiting membrane all of which appear to resist postmortem autolysis for longer periods of time.

Despite the fact that microscopic and ultramicroscopic alterations in structure are not seen in the internal limiting membrane and ciliary epithelium in this series of experiments, the gross dilatation of the ciliary ring remains to be explored in greater detail.

IV. Lens capsule

In this series of experiments comparison of the stained sections does not reveal any significant changes in thickness or in staining reaction of the lens capsules of enzyme-treated eyes, either human or monkey.

The relatively great variations in the thickness of the normal lens capsule precludes comparison of electron micrographs of treated and control eyes for possible enzyme-induced alterations in thickness of the capsule. However, electron microscopic study of the finer details show that in some sections near the equator there is a pericapsular membrane identical in structure with the zonules. It may be only a continuation of the zonules since it is not demonstrable in the central portions of the capsule. This superficial or pericapsular portion is seen to be fragmented after enzymatic zonulolysis in a pattern identical with zonular fibrils. On the other hand, the capsule proper of the enzyme treated eyes does not show any alterations in its dense basic structure (such as fragmentation of its fibers or vacuolization) even under scrutiny of the electron microscope.

The lack of histologic evidence of lens capsular changes here is of considerable interest in light of the report by Clement[2] that the lens capsules of lamb, rabbit and cattle eyes after zonulolysis with alpha chymotrypsin are weakened by a factor of 10 or more. Resistance of the capsule to vacuum was used by Clement as a measure of its strength. One important difference should be pointed out, namely, the concentrations of alpha chymotrypsin used by Clement were 1:1,000 and 1:2,000—10 times the concentrations used here.

It is apparent that much further work remains to be done. Biochemical studies as well as mechanical tests such as performed by Clement for possible alterations in strength of the capsule should be done on human and monkey eyes using 1:5,000 and 1:10,000 dilutions of alpha chymotrypsin. It is conceivable that chemical alterations in lens capsule which might weaken it may escape notice in the fixed histologic preparations.

Summary and Conclusions

1. Alpha chymotrypsin in dilutions of 1:5,000 and 1:10,000 produces a selective disintegration of the zonules characterized by fragmentation of the component fibrils into uniform segments of approximately 1,000 Å. in length.

2. The enzymatic zonulolysis begins with thinning and stretching of the zonules which take place promptly within three to five minutes.

3. The initial stretching of the zonules is accompanied by dilatation of the ciliary ring and a forward protrusion of the lens and vitreous.

4. The anterior hyaloid face and its attachment to the posterior capsule of the lens does not appear to be affected by exposure to the enzyme for periods far in excess of that required for complete disintegration of the zonules.

5. The lens capsule, internal limiting membrane and ciliary epithelium show no microscopic changes following zonulolysis by alpha chymotrypsin.

6. In comparison of human and monkey eyes no species differences were noted in response to the enzyme.

7. The 1:10,000 dilution of alpha chymotrypsin was not noticeably less effective than the 1:5,000. The only failure to produce zonulolysis occurred in a younger animal in which the stronger (1:5,000) dilution was being used.

640 South Kingshighway (10).

REFERENCES

1. Barraquer, J.: Zonulolisis enzymatica. An. Med. & Cirugia, **34**:148 (July-Aug.) 1958.
2. Clement, F.: Experimental studies of zonulolysis. Read at IV Reunion of Spanish Physiological Society May 29-31, 1958.
3. Holmberg, Å.: Differences in ultrastructure of human and rabbit ciliary epithelium. Arch. Ophth., in press.
4. ———: Ultrastructure of the ciliary epithelium. Arch. Ophth., in press.

CLINICAL TONOGRAPHY*

WITH AND WITHOUT A RECORDING GALVANOMETER

WINSTON ROBERTS, M.D.
Winston-Salem, North Carolina

The place of tonography in the clinical handling of glaucoma is by now sufficiently well documented to require little further emphasis. Those who have used it extensively feel that it is an essential aid to diagnosis in early glaucoma, to classification in equivocal cases, to evaluating the efficacy of therapy in simple glaucoma, and as an aid in the determination of the type of surgery needed in closed-angle glaucoma.

* From the Department of Ophthalmology, Bowman Gray School of Medicine. This study was supported by a grant from the U. S. Public Health Services (National Institute of Neurological Diseases and Blindness, B-213).

TONOGRAPHIC CRITERIA FOR DIAGNOSIS OF GLAUCOMA

C-value repeatedly below 0.19. After water-drinking provocative test: C-value falls below 0.18—0.19 or markedly below usual level. Po/C>100.

After pupillary dilatation: C-value subnormal or lower than usual.

The tonographic diagnostic criteria in the preceding paragraphs are considered valid aids in establishing a diagnosis of glaucoma, when tonography is used both with and without accompanying provocative tests.[1] These include C-values persistently or repeatedly

below 0.19, a C-value which falls to subnormal levels or shows a marked drop from previously established normal levels for the individual after water-drinking provocative where simple glaucoma is suspected and after pupillary dilatation where closed-angle glaucoma is suspected,[2] and a Po/C ratio of more than 100[3] after water-drinking. Tonography done as a part of provocative testing should usually be accompanied by gonioscopy to clarify the classification in these cases.

Tonographic criteria for therapy of simple glaucoma

C = 0.20 or better—90 + percent field retained; C = 0.15 or better—82 + percent field retained; Po/C < 100—90 + percent field retained.

Angle-closure glaucoma

C normal after T normalized medically usually justifies iridectomy.

The preceding paragraphs outline the present criteria for therapeutic efficacy as determined from tonographic data. Becker[4] has pointed out that normalization of the C-value (facility of aqueous outflow) will give approximately 90 percent certainty of protection against field loss in simple glaucoma. C-value of 0.15 will lead to retention of fields in 82 percent, and where a Po/C ratio of less than 100 is established by medical therapy, field retention can be expected in something better than 90 percent of all but advanced glaucoma cases. In addition, where the C-value rises to normal levels after the tension is normalized by medical means in closed-angle glaucoma, a conservative iridectomy appears fully justified as surgical treatment in this glaucoma.

All these useful applications of tonography in clinical work presuppose that the tonography is done with impeccable technique. To most of those who have dealt with tonography extensively, this implies careful training of both the operator and the patient so that extreme gentleness, freedom from tension, careful placing of the electronic tonometer, and an easy, restful fixation device must be used. In addition, accuracy implies the use of a recorder, with sufficiently high sensitivity to picture accurately any physiologic or other effect on the tonogram, or to disclose any malfunctions of the tonometer, operator, or patient by faulty tracing which can readily be observed. It is felt by those who have developed this technique that the tonogram is a reflection of a fall in tension resulting from the expression of aqueous by the weight of the indenting tonometer plunger, and that this fall can be expressed as an essentially linear equivalent of the oscillating tracing on the recorder. It would appear that the normal tonogram can be represented by a slightly curved linear equivalent, tending to flatten as the basal pressure is approached, while in the glaucomatous eye, the tonogram becomes both flatter and straighter in most cases. The validity of tonography with a recorder as a measure of efficiency of aqueous flow has been established by its correspondence to other techniques for this measurement, such as fluorescein appearance time, and perfusion studies.[5, 6]

It has been proposed by some that tonography satisfactory for clinical purposes can be performed without the use of a recording galvanometer simply by taking repeated readings, at one-half minute intervals or more frequently, from the hand of the tonometer so that the averages can be determined from these readings. For practical purposes in clinical work, the C-value may readily be determined by taking the initial and four minute readings as determined from the linear equivalent of the tracings, or the initial and four-minute readings taken from direct reading, and from published graphic diagrams[7] the C-value can readily be estimated, or if it is preferred, mathematical calculation can be made using the by now familiar formula:

$$C = \frac{\Delta V}{t\,(Ptav\text{-}Po\text{-}\Delta PV)}$$

The present study was undertaken as a part of a more extensive early glaucoma

study, to attempt to determine definitively how nearly tonography done from direct readings from the tonometer might be expected to correlate with values obtained from the galvanometer recordings, which are assumed to be the most nearly accurate data for determining the C-value with this useful technique which admittedly contains considerable possibilities for experimental error. Those who have felt that direct readings will too often be misleading have pointed out the not infrequent wide swings which the hand of the tonometer may make as a result of respiratory and other physiologic changes in the patient, or from tension of the patient's eyelids, not to mention technical difficulties with the apparatus, all of which are readily disclosed by the recording.

Figure 1 demonstrates the typically good tracing in which a relatively uniform fall in tension occurs, and in such a tracing it might be expected that direct readings will produce a very nearly satisfactory evaluation of the facility of outflow.

On the other hand, such tests as those in Figure 2, which show an obviously unphysiologic drop, particularly in the first half minute or so of the test, or those in Figure 3, which show malfunction of patient and instrument, would make accurate direct readings difficult if not impossible. It can be stated that a skillful technician, whose sophistication relative to the test is high, should come much nearer reading the tonometer accurately, and from the columns of figures which are set up also make corrections in these columns, as will be indicated later, which will make it possible to approximate more nearly accurate results, but such corrections are even more subject to human error than determinations taken from a recording.

The material from this comparison consists of tonographies done on 150 patients with either proved early glaucoma or suspected glaucoma. Of the 150 cases, 38 were called equivocal because the diagnosis was not thoroughly established at the time of this study, or because the cases were not considered to be glaucoma. The other 112 cases

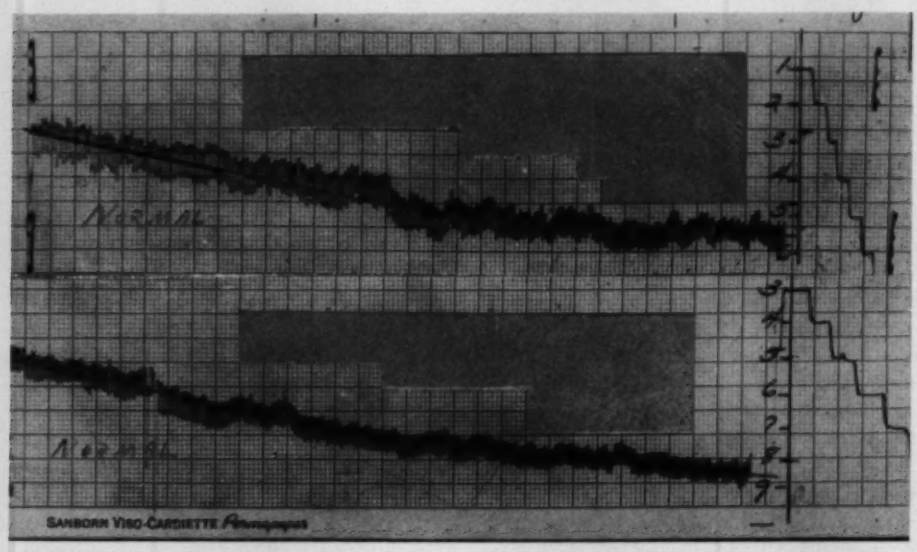


Fig. 1 (Roberts). A typically good tracing. (Above) O.D., C = 0.27; Po/C < 100. (Below) O.S., C = 0.28; Po/C < 100.

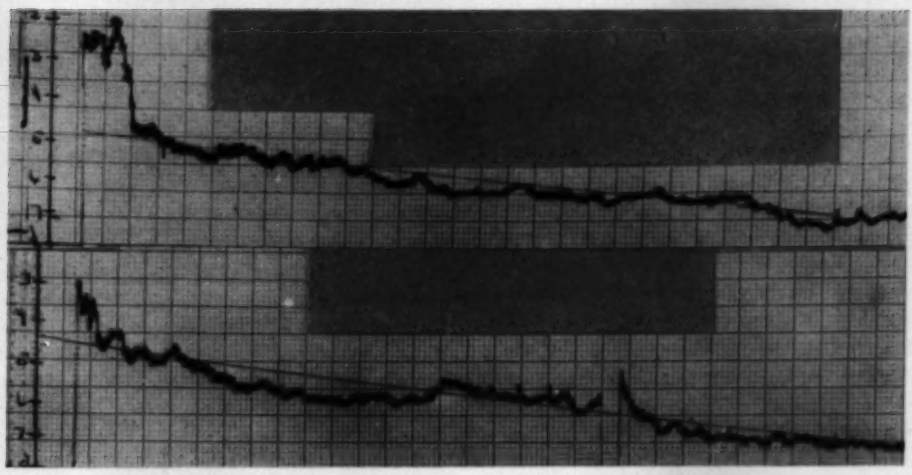


Fig. 2 (Roberts). Showing an obviously unphysiologic drop. (Above) O.D. High initial reading. C = 0.14 (one-half to four and one-half minutes). (Below) O.S.

were all considered primary glaucoma: 21 were closed-angle glaucoma; four were hypersecretion glaucoma; two were juvenile glaucoma; and 85 cases were simple glaucoma.

A total of 790 tonographies were done. Simultaneous galvanometer recordings and direct readings taken from the tonometer at half-minute intervals were made in all instances. Of these 790 tonographies, 146 were done in the equivocal group, 105 in the closed-angle glaucoma group, 501 in the simple glaucoma group, 30 in the hypersecretion group, and eight in the juvenile glaucoma group.

For the purposes of the statistical analysis of these tonographies, the juvenile and hypersecretion cases were grouped with the simple glaucoma, since otherwise numbers were considered too small for significant analysis.

In addition, on 61 tonographies with more or less random distribution among the above groups, where very wide discrepancies existed between the C-value estimated from the linear equivalent of the tracing and that estimated from the initial and four-minute readings taken directly from the tonometer, a corrected value for the direct readings from the tonometer was estimated by using the

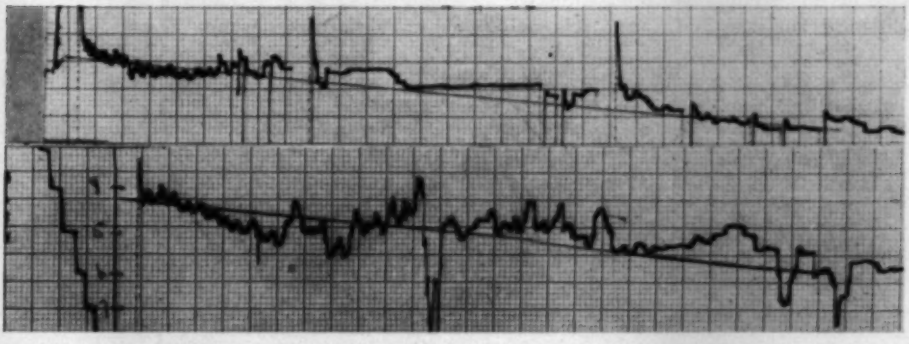


Fig. 3 (Roberts). Showing malfunction of patient and instrument (Above) O.D. (Below) O.S.

TABLE 1

MAXIMUM DEVIATIONS BETWEEN C_1 AND C_2

	Deviation	No. Cases
Equivocal	0.22	146
Closed-angle	0.16	105
Simple	0.22	501
Hypersecretion	0.23	30
Juvenile	0.05	8
Group IVb (Corrected)	0.22	61

half-minute and four and one-half-minute readings, or the one-minute and five-minute readings, if these seemed to fit better into a linear distribution with the other readings taken from the tonometer.

In all tables, values listed as C1 will be the facility of outflow determined by the galvanometer recordings, C2 the facility of outflow determined from the initial and four-minute readings taken directly from the tonometer, and in the corrected group, C3 will indicate the corrected readings taken at other than initial and four-minute intervals.

If the assumption is made that the facility of outflow as measured by a well-performed tonography with a recording galvanometer under well-controlled conditions is a reasonably valid measure of function, which seems reasonable in the light of evidence now repeatedly presented, the purpose of this study would be to evaluate how nearly tonographic values taken from direct readings from the tonometer can be expected to approach those taken from the accepted technique with the recording galvanometer. For this purpose the data in this study have been subjected to statistical analysis, and from this analysis certain relationships may be presented.

First, the maximum deviations between the C-values obtained by the two methods in the different groups are indicated in Table 1.

While the data in Table 1 are selected extreme deviations from each group and are accordingly nonrepresentative, they do point out that in every group except the juvenile group, which is entirely too small to be of analytic value, the deviation between the two methods may be quite large, and the less valid method may lead to false diagnostic or therapeutic indications. Even in the so-called corrected group, the maximum deviation between the two values reached a high level equivalent to those seen in the other groups, although in general values here appear to approximate each other.

A comparison of data obtained from the recordings and from direct readings from the tonometer begins in Table 2. Here the mean differences, probable errors in the estimates of the mean differences, and the standard deviations are listed by the groups into which the tonographies fall. If both techniques provide equally valid measure of facility of outflow, one would expect that the mean differences between simultaneous tests would not differ significantly from zero. It can readily be observed that, in general, the probable error in the mean is lowest in the series in which there are large numbers of tonographies, and in particular in the simple glaucoma group (Group 3). However, as data in Table 2 indicate, in all groups the mean difference deviates significantly from

TABLE 2

COMPARISON OF DATA

Classification	No.	Mean Difference*	Probable Error in Mean	Standard Deviation
Group I (equivocal)	146	0.037	0.0023	0.041
Group II (closed-angle)	105	0.038	0.0023	0.035
Group III (simple, etc.)	539	0.035	0.0001	0.036
Group IVa	61	0.113	0.0317	0.357
Group IVb	61	0.032	0.0047	0.037
TOTAL (except IVa & b)	790	0.036	0.009	0.037

* t—test of differences suggests that all mean differences deviate significantly from zero.

TABLE 3

CORRELATION COEFFICIENTS

Group	No.	Correlation Coeff.
Group II—Closed-angle	105	0.803
Group III—Simple	539	0.798
Group I—Equivocal	146	0.763
Group IVa—Poor values	61	0.405
Group IVb—Poor values corrected	61	0.701
TOTAL (except Group IV) (1 = perfect correlation)	790	0.786

zero (probability < 0.001, except in Group IVa where probability < 0.025).

The variation between two simultaneous tests springs from three sources: (1) variations between individuals (common to both tests), (2) experimental error in the two techniques, and (3) random or uncontrolled variation. A second statistical approach, correlation analysis, provides us with a measure of the proportion of variation which is common to both tests, that is, variations due to differences between individuals in the facility of outflow. Even if the two tests measured the same characteristic with equal reliability, experimental and random errors would prevent one's obtaining a perfect correlation ($r = 1$). On the other hand, unless results of the two tests show a high correlation, the two tests will not be equally useful as clinical tests of facility of outflow. The proportion of variation common to both test procedures (r^2) and the proportion of variation attributable to experimental errors and random variations in each test ($1 - r^2$) provide independent information on the predictive value of the two tests relative to each other.

The correlation coefficients calculated for each group are presented in Table 3. It is apparent from these data that even the largest coefficient found (0.803 for Group II) is not high for two techniques which purport to measure the same characteristic. Sixty-four percent of the variability (0.803^2) is the result of common elements, that is, variations between individuals, while 36 percent results from differences in the two techniques, experimental errors, and random variations. Present data do not permit us to separate experimental and random errors from variations due to real differences between the two techniques. However, coefficients of variation computed for each test indicate that direct reading values are more variable than values obtained using the galvanometric method. The correlation coefficients for Groups I and III are only slightly below that obtained for Group II. However, the coefficient for Group IVa is significantly lower than that for any other group. This fact is not surprising because that group was selected using poor agreement between the two tests as a criterion. More importantly, it can be noted that the coefficient for the corrected group (IVb) is significantly lower than those of Groups I, II, and III. This difference suggests that the method of correction was not able to correct completely major discrepancies. Furthermore, all of the coefficients suggest that clinicians could not predict with great confidence the value which would be obtained using one technique from a value obtained using the other.

A final evaluation procedure was to calculate the distribution of mean differences presuming that they would follow the normal curve. These data are presented in Table 4. The accuracy of fit between the observed

TABLE 4

DISTRIBUTION OF DEVIATIONS

TOTAL GROUP

Difference	Expected No. in Normal Curve	Observed No.	$\chi^2 = \frac{(o-e)^2}{e}$
0.00–0.04	572.1	544	1.38
0.05–0.09	206.7	184	2.49
0.10–0.14	11.1	48	230.41
0.15–0.19	0.1	10	
0.20+	0.0	4	
TOTAL	790.0	790	234.28

TABLE 5

DEVIATIONS BY GROUPS

Difference	Group I—(Equiv.)		Group II—(Closed)		Group III—(Simple)	
	Observ.	Expect.	Obs.	Ex.	Obs.	Ex.
0.00–0.04	90	102.4	70	77.4	361	379.8
0.05–0.09	40	40.8	25	26.4	108	116.9
0.10–0.14	14	2.7	7	1.2	23	4.3
0.15–0.19	1	0	3	0.0	6	0.0
0.20+	1	0	0	0.0	3	0.0
TOTALS	146	146.0	105	105.0	501	501.0

and expected distributions was calculated using the Chi-square test. It is highly improbable that the deviations between expected and observed is due to chance (probability < 0.001). The major contribution to the X^2 (Chi) value arises from the excessive number of large deviations. The significant difference between the two distributions implies that there is some basic difference in the two techniques which would appear to make the use of one or the other method unreliable for the measurement of the facility of aqueous outflow.

Table 5 presents the individual groups treated in a similar fashion. These data indicate that the excess of wide discrepancies is not contributed by a specific group but arise in every group, a fact which supports the idea that the discrepancies arise because of differences in the two techniques rather than differences in individuals or groups. A further analysis of the frequency of abnormal values in individuals who were tested repeatedly gave no evidence that particular individuals were responsible for a disproportionate number of wide discrepancies.

DISCUSSION

In considering the comparison of the data obtained from the tonographies done by the two different methods, it should be re-emphasized that in all cases the data were obtained on the two methods simultaneously, since in each case the recordings and the direct readings from the tonometer were done simultaneously during the performance of any given tonography. Therefore, any physiologic or technical difficulties had an equal opportunity to affect both methods, and poor correspondence between the two methods must lie in faults or errors of one or the other method.

Since the validity of the tonogram as performed by the standard technique with a recording galvanometer has been well substantiated previously by good correspondence with other techniques for measuring aqueous flow, it would appear that the source of the large error must come from the direct reading technique. The high excess of large deviations above the number expected from a random or "normal curve" distribution appears to be due chiefly to readings taken on wide swings of the tonometer hand away from the general linear curve of the tonogram. These wide swings are most prone to occur in the first one-half minute to one minute, where the effect on the facility of aqueous outflow as determined from the initial and four minute readings is greatest. Such errors may lead to completely faulty placing of a C-value in the normal glaucomatous population curve and consequent completely faulty handling of a clinical case, if the C-value determined from erroneous direct readings is accepted at face value.

On the other hand skilled reading from the tonometer may minimize such errors, and expert interpretations of the group of readings taken directly from the tonometer may make possible smoothing out some of the gross errors. Under any circumstance, how-

ever, such corrections are unreliable and excessively susceptible to subjective interpretation by the technician. This would appear to indicate that tonography done by direct readings from the tonometer is a technique with excessive inaccuracy, and should be used only where the proper set-up with recording galvanometer is impossible.

Summary

1. A total of 790 tonographies, done on 150 cases of early glaucoma or glaucoma suspects, were simultaneously checked with the facility of aqueous outflow, both from galvanometer recordings and from repeated direct readings taken at one-half minute intervals from the tonometer hand.

2. Comparison of the two methods has revealed unsatisfactory correlation between the two, with an excessive number of large deviations between the two techniques.

3. The excessive deviations and faulty correspondence between the two methods appear to be chiefly a function of inaccuracies in the direct-reading technique which would, therefore, seem to be an essentially unsatisfactory substitute for the standard technique for tonography.

Department of Ophthalmology,
Bowman Gray School of Medicine.

Appreciation is expressed to Dr. H. O. Goodman, Bowman Gray School of Medicine, for the statistical analyses of data in this paper, and for his help in their interpretation.

References

1. Roberts, W., Becker, B., et al.: In Glaucoma: Transactions of the Third Conference (Edited by F. W. Newell), New York, Josiah Macy, Jr., Foundation Publications, to be published.
2. Becker, B., and Thompson, H. E.: Tonography and angle-closure glaucoma: Diagnosis and therapy. Am. J. Ophth., **46**:305, 1958.
3. Becker, B., and Christonsen, R. E.: Water-drinking and tonography in the diagnosis of glaucoma. Arch. Ophth., **56**:321, 1956.
4. Becker, B.: The prognostic value of tonography in the miotic therapy of chronic simple glaucoma. Am. J. Ophth., **46**:11, 1958.
5. Bárány, E. H., and Wirth, A.: An improved system for estimating rate of flow of aqueous humor in individual animals. Acta Ophth., **32**:99, 1954.
6. Goldmann, H.: Abflussdruck, Minutenvolumen, und Widenstand der Kammerwasserstromung des Menschen. Docum. Ophth., **6**:278, 1951.
7. Ballintine, E. J.: Clinical tonography. Rochester, Minn., Acad. Ophth., 1954.

LIGHT COAGULATION*

DuPont Guerry, III, M.D., and Herbert Wiesinger, M.D.
Richmond, Virginia

Three years ago, our first experimental results on the effects of high intensity visible light on the retina and choroid were presented before the American Ophthalmological Society.[1] This study had been carried out for the Air Force[2] and while our primary concern was with the hazards resulting from the light flashes of atomic explosions, it was at once evident that light coagulation should prove to be a valuable clinical tool. This had already been suggested by Dr. Meyer-Schwickerath of Bonn, Germany, who had used sunlight as a source of energy as early as 1948 in the clinical treatment of various types of fundus lesions. At the International Congress in 1954 in New York he reported on the treatment of such lesions with a light coagulator in which a high-intensity Xenon arc served as light source.[4-9]

* From the Department of Ophthalmology, Medical College of Virginia. This work was sponsored by a grant from the Knights Templar Eye Foundation, Inc. Presented at the 95th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1959.

Three years ago we had the good fortune of finding a von Hippel's angioma of the macula in the right eye of a patient which was successfully treated with our experimental machine. With this apparatus only the macular area could be treated since, in order to carry out coagulation, it was necessary for the patient to look directly into the light. Peripheral lesions could not be treated with this apparatus because of the great difficulty in localizing the area to be treated. This case was reported in THE AMERICAN JOURNAL OF OPHTHALMOLOGY for October, 1958.[3]

Following the successful treatment of this case, the potentialities of this form of treatment became even more apparent. Plans were made for developing a clinical instrument when it was learned that Dr. Littman of the Zeiss Company had designed a light coagulator for Dr. Meyer-Schwickerath which would soon be made available commercially. After corresponding with Dr. Littman and Dr. Meyer-Schwickerath and after sending two members of our department to Germany, we were able to obtain a light coagulator for the Department of Ophthalmology at the Medical College of Virginia. This instrument was installed and ready for use in May, 1958. This presentation summarizes our results during the past year in employing this instrument, both experimentally and clinically.

Prior to using this instrument clinically, it was calibrated with the same water flow calorimeter as was used in calibrating our experimental instrument. When this was done, it was found that the Zeiss instrument could develop an irradiance up to 1.9 cal./cm.^{2}/sec. when measured at the cornea (about 30 to 40 percent more energy than that available with the experimental machine). When translated into maximum energy available at the retina, this proved to be 95 cal./cm.^{2}/sec. for an image of 1.0 mm. size.

After calibrating the instrument, a number of rabbits were burned and it was found that rather severe chorioretinal burns could be obtained with a very short exposure time and with much less intensity than the maximum. It was also found that when maximal or somewhat submaximal intensity was used with even a short exposure time a popping noise could be heard, the noise resembling that heard when corn pops. This was found to be due to a sudden massive build up of steam within the confines of the choroid and retina which exploded into the vitreous, leaving a crater which could be seen ophthal-

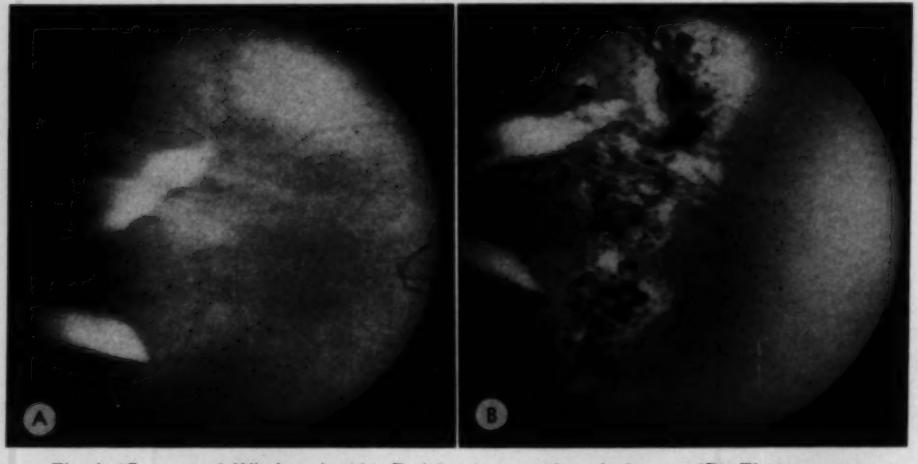


Fig. 1 (Guerry and Wiesinger). (A) Peripheral traumatic retinal tears. (B) The same case three weeks after light coagulation.

moscopically. Minimal burns could be obtained in the rabbit with the least intensity available on the machine and with an exposure time of about 0.5 second.

After employing the machine for several weeks in animal experiments, it was felt that enough experience was available for us to tackle our first human case. As might be expected, the first candidate proved to be a doctor. This individual had suffered two previous detachments and had developed a hole in the midperiphery, in an area of old lattice degeneration. This brave lad felt that light coagulation was preferable to diathermy and immediately volunteered. A delimiting barrage was laid down surrounding the area of lattice degeneration and the hole itself coagulated; immediately thereafter the patient was able to return to work.

In this case, and in the others that followed, it became apparent that considerably more energy was necessary for a burn of the human choroid and retina than was necessary for a burn of similar severity in the rabbit (about one-half again as much energy). Since this initial case, light coagulation has been carried out on 42 eyes. These fall into several different categories:

1. *Retinal tears with or without flat detachment* (figs. 1—A and B and 2). Retinal tears of traumatic or degenerative origin with no detachment or very early flat detachment lend themselves beautifully to light coagulation therapy. The area of the tear should

Fig. 2 (Guerry and Wiesinger). Spontaneous retinal tears in midperiphery two days after light coagulation.

be sealed off first by a barrage laid down at the periphery of the tear where the retina is absolutely flat and where there is no separation. The area of the tears themselves should then be burned and in such cases the minimal amount of subretinal fluid present absorbs without further therapy. About seven days postexposure a firm pigmented barrage can be seen ophthalmoscopically and its appearance differs in no wise from that produced by diathermy. We have so far treated nine cases of this type with excellent results.

2. *Delimiting barrage in old detachments* (figs. 3—A, B and C). One case of a large moderately elevated old inferior detachment

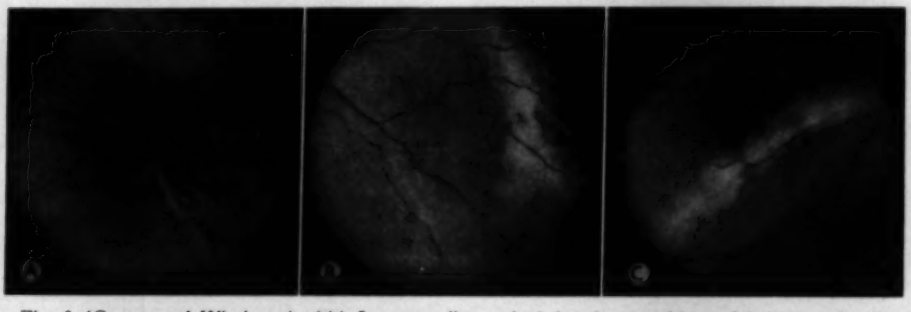


Fig. 3 (Guerry and Wiesinger). (A) Long-standing retinal detachment with partial demarcation line. (B) Same area immediately following a delimiting barrage with the light coagulator. (C) Delimiting barrage in another area of the same eye.

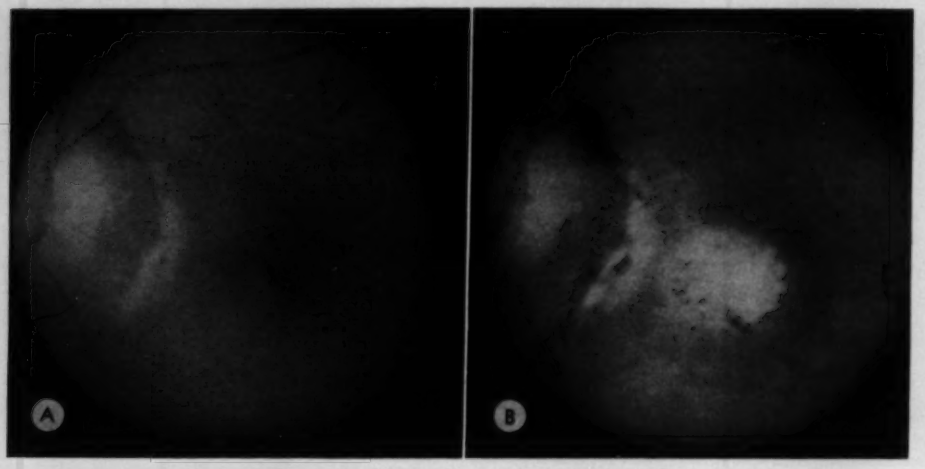


Fig. 4 (Guerry and Wiesinger). (A) Macular hole with retinal folds. (B) Same case one week after light coagulation.

with encroachment on the macula and with beginning spontaneous demarcation lines was treated successfully in a 16-year-old boy. Central vision was preserved.

3. *Macular holes or cysts* (figs. 4—A and B, 5, 6, and 7). Macular holes or cysts, of either primary or secondary etiology, are naturals for this type therapy. It must be emphasized, however, that for light coagulation to be successful the area of the hole must be flat, else coagulation will not occur. It is, therefore, important to treat these lesions early before separation has occurred and if there is actually a detachment present, fluid must be evacuated before attempting coagulation. In all instances of this type lesion visual acuity has long since gone by the board and, as a consequence, impairment of central vision is not a problem. Five macular holes or cysts were successfully treated and two cases were treated unsuccessfully. In these cases the area of the hole and a small amount of the surrounding retina was coagulated.

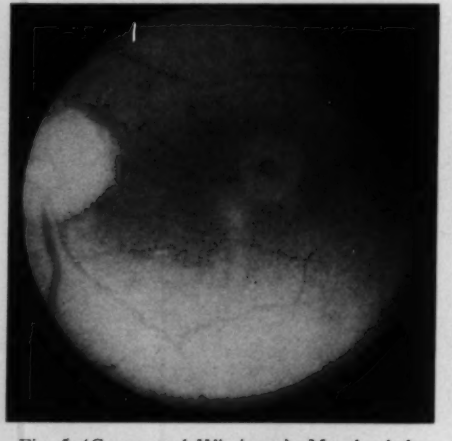


Fig. 5 (Guerry and Wiesinger). Macular hole immediately after light coagulation.

In the first unsuccessful case the hole was of traumatic origin and the entire retina was detached and elevated from two to three diopters. Mild coagulation did not result in a take, but after coagulation with moderately strong intensity an apparent adhesion resulted. The retina did not remain flat and after a couple of weeks it redetached. It was not possible then to carry out coagulation with the light coagulator as the detachment had become bullous. Drainage of subretinal fluid, followed by injection of vitreous, was then tried and when this failed an Arruga type cinching procedure was carried out, but without success. The other case failed be-

cause of moderate elevation of the central retina and the patient refused further surgery.

4. *Combined surgery and light coagulation.* In nine cases of retinal detachment, where the retina was bullous or moderately elevated, conventional diathermy with evacuation of fluid and treatment of the holes with diathermy was carried out and at the end of surgery, or several days postoperative, the light coagulator was used to supplement the diathermy barrage. A preoperative delimiting barrage was employed in four of these cases to prevent possible spread of the detachment to the macular area. In one instance, where there had been two previous detachments in an aphakic eye followed by scleral resection and reattachment, a successful reattachment occurred following a complete circumferential light barrage laid down inside the ring of scleral resection and supplemented by vitreous injection. Vision obtained in this case was the same as that noted prior to the last detachment (20/70).

Another interesting case in this group was that of a 72-year-old man, who had undergone a previous detachment operation, a cataract extraction and a glaucoma operation in the affected eye. When the retina again detached he was found to have two small holes, one immediately below the disc and another in the 6-o'clock meridian just inside the ora. An attempt was made to seal the small hole near the disc with the light coagulator, but it was found that subretinal fluid prevented a take. Subretinal fluid was then evacuated in the lower periphery and at the same time a surface diathermy barrage was laid down over the lower half of the retina two to three mm. posterior to the ora. The sclera over a degenerated area very close to a vortex vein was coagulated with diathermy. As the fundus was observed following this, a spontaneous choroidal detachment was seen to creep in from this peripheral area and to embrace completely the hole below the disc. When light coagulation was then carried out the hole was easily sealed off. The area of the hole in the periphery was also treated with ease by the light coagulator. Following this treatment, the patient obtained 20/30 vision with correction which was the same acuity he had prior to detachment.

This very interesting case suggested to us the possibility of draining subretinal fluid and at the same time creating a spontaneous choroidal detachment which would push the

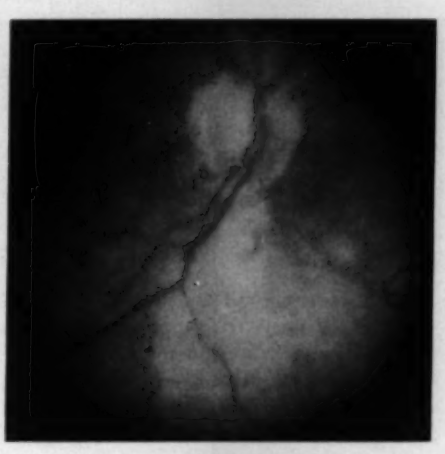


Fig. 7 (Guerry and Wiesinger). Small retinal hole below the disc immediately after closure with light coagulation.

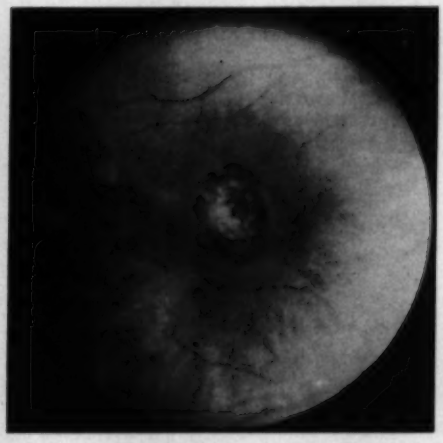


Fig. 6 (Guerry and Wiesinger). Another macular hole two weeks after light coagulation.

choroid against the area of the retina where light coagulation could then be carried out. Such a procedure has been tried on several eye-bank eyes with success and will shortly be tried on a suitable detachment case. As yet it is not apparent whether fluid injected into the suprachoroidea will be the most effective method of causing a choroidal detachment, but this at present appears to be the most feasible.

Recently a case referred to us with a recurrent detachment following a Schepens encircling tube was successfully treated. A hole had developed on the surface of the tube and a flat detachment was beginning to spread from this area toward the macula. With the light coagulator the detached area was completely sealed off, although the hole itself could not be sealed since the buckled area over the hole would not absorb sufficient heat to cause coagulation. This phenomenon is apparently due to two causes:

1. In tubed cases of long standing the choroidal pigment becomes atrophic over the tube.

2. The tube itself is transparent. Thus, there is no pigment to absorb the light resulting in coagulation: instead the light passes through and is dissipated.

If one expects to employ the light coagulator in tubing operations of this sort, it would seem advisable to use a darkly pigmented tube, instead of a transparent one, as a substitute for the atrophic choroid. If tears then occur on the surface of the tube, coagulation can be carried out, not only in the area of the detachment itself, but in the region of the buckled hole.

5. *Tumors of the retina and choroid* (fig. 8-A, B, C). Lesions of this type lend themselves beautifully to light coagulation. Von Hippel's hemangioma can be easily treated with the light machine, but where the tumor is of massive size it should be eradicated slowly by repeated exposure at intervals of two to three weeks. At the present time we are treating a massive hemangioma involving about a third of the retina. This patient has been treated at monthly intervals for five months and the tumor now is about a third of its original size.

It is important to remember in these large tumors that the tremendously dilated and tortuous feeder vessels should be assiduously avoided, for if they are inadvertently burned, a rupture may take place either at the time of the burn or later by necrosis. As a result of this the vitreous cavity will be flooded by blood which, of course, precludes further light coagulation, at least until such time as the blood absorbs. We have not yet run into this difficulty, but we were emphatically warned about it by Dr. Meyer-Schwickerath. A hemangioma of the choroid was treated with our light machine for Dr. Angus MacLean by Dr. Meyer-Schwickerath. This case

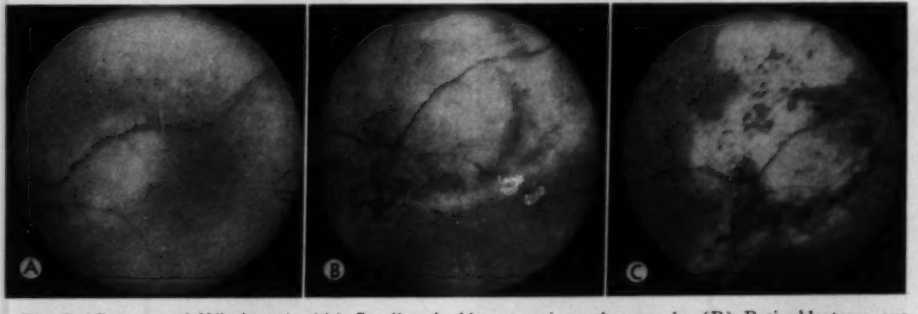


Fig. 8 (Guerry and Wiesinger). (A) Small retinoblastoma above the macula. (B) Retinoblastoma one week after light coagulation. (C) Same retinoblastoma four weeks after first and one week after second light coagulation.

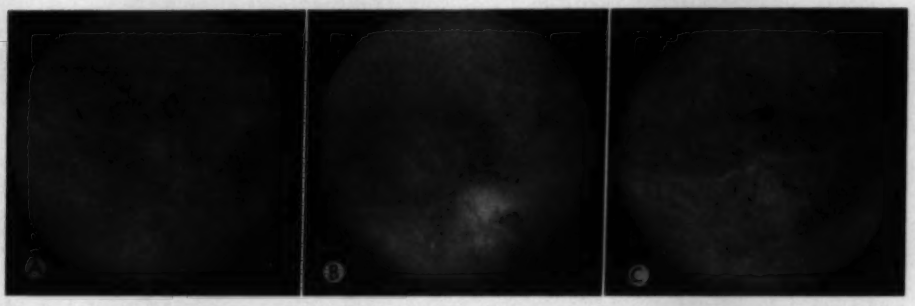


Fig. 9 (Guerry and Wiesinger). (A) Retinal neovascularization following central vein occlusion. (B) Same area immediately after light coagulation. (C) Same area one month after light coagulation.

has been reported by Dr. MacLean.[10]

Recently, treatment was begun on a case of Coats' disease associated with numerous aneurysms and neovascularization in the periphery. The large size of involvement of the retina has necessitated the multiple-staged approach and at the present time only three treatments have been carried out. However, rather remarkable shrinkage has already occurred.

We have not yet had a malignant melanoma to treat but Dr. Meyer-Schwickerath, in his paper at the International Congress in Belgium,[8] reported success in 43 out of 63 clinical melanomas which he treated. None of these was larger than six or seven disc diameters in size.

Small retinoblastomas involving less than a quarter of the retina can be treated by light coagulation. We have had experience with only one such tumor which occurred in an 18-month-old child whose right eye had been enucleated two weeks prior because of a massive retinoblastoma, proved histologically. At the time of this surgery the referring doctor had found a small retinoblastoma two disc diameters in size about three disc diameters above and temporal to the macula. A circumferential barrage was laid down surrounding this tumor and then the tumor was coagulated with greater intensity. One week later the tumor was again coagulated and three weeks later a large pigmented scar could be seen in the area where the tumor had been, but in the center there was still a small nonpigmented zone. It was felt that to be safe further light coagulation should be carried out and the depigmented zone was again treated with a fairly intense dose. The involved area now is reduced to a large mottled

Fig. 10 (Guerry and Wiesinger). (A) Recurrent central chorioretinitis with two active lesions. (B) Same case immediately after light coagulation. (C) Same case two months after light coagulation.

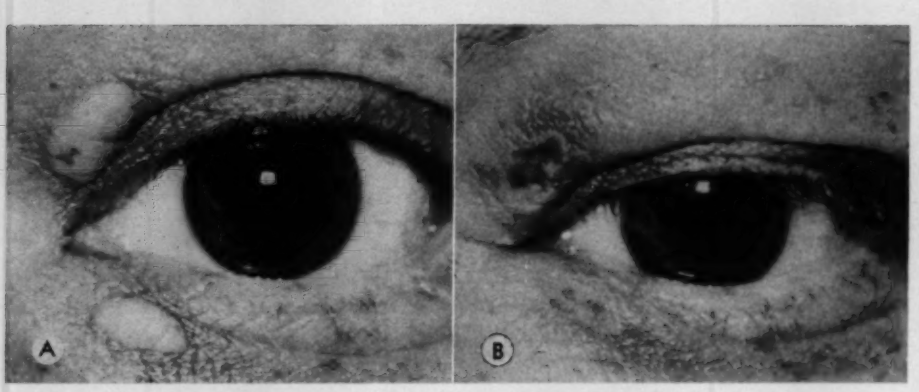


Fig. 11 (Guerry and Wiesinger). (A) Xanthelasmas. (B) Xanthelasmas immediately following treatment with external light coagulation.

pigmented area similar to that seen in areas of old choroiditis and there is no evidence of tumor.

6. *Retinal neovascularization* (fig. 9-A, B. C). One case of retinal neovascularization following venous obstruction has been treated with a good result. This was done prophylactically to prevent repeated hemorrhages.

7. *Central retinal schisis.* Two cases of central retinal schisis following disciform mascular degeneration were also treated prophylactically. In the past we have seen on several occasions a complete detachment resulting from lesions of this type and for this reason prophylactic coagulation was carried out. Both of these lesions were successfully walled off.

8. *Solitary or sharply localized areas of acute choroiditis* (fig. 10-A, B, C). It would seem that this type lesion would be most responsive to light coagulation. Four cases were so treated, two apparently with success and two unsuccessfully. Strangely enough, the two which were apparently successful were of the type thought to be toxoplasmic where daughter lesions constantly recur. In these instances both the old lesions and the fresh were coagulated. In both cases of failure the

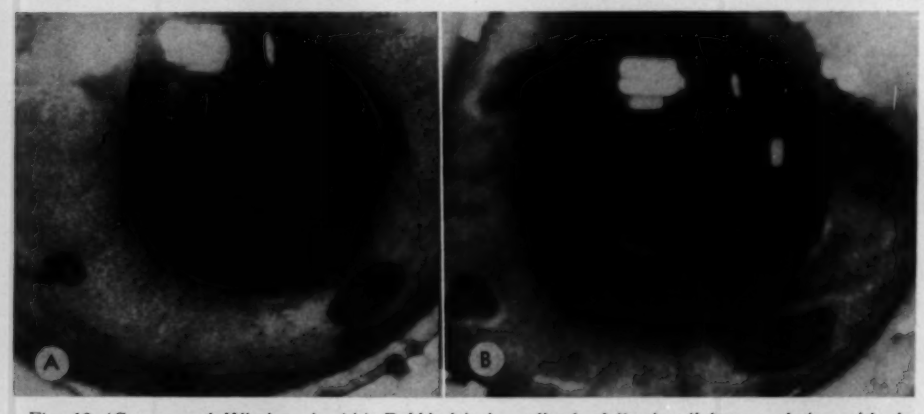


Fig. 12 (Guerry and Wiesinger). (A) Rabbit iris immediately following light coagulation with the external light coagulator. (B) Same rabbit after one month. In two of the coagulated areas a hole has formed in the iris.

TABLE 1

LIGHT COAGULATION

	No. of Cases	Result		
		Good	Poor	Insufficient Follow-up
1. Retinal tears without or with flat detachment	9	8		1
2. Delimiting barrage in old detachment	1	1		
3. Macula holes	7	5	2	
4. Combined surgery and coagulation	9	7		2
5. Tumors	4	2		2
6. Neovascularization of retina	1	1		
7. Central retinal schisis	2	2		
8. Choroiditis	4	2	2	
9. Xanthelasmas	3	3		
10. Artificial pupil	2		1	1
Total	42	31	5	6

lesion was a solitary one. In both of these cases there were probably additional peripheral lesions which could not be found.

9. *Light coagulation with the external coagulator* (fig. 11-A and B). The adapter for light coagulation of external lesions of the eye has only been in our possession for about three months. During this interval we have burned several xanthelasmas, all with good results. Following light coagulation of the xanthelasmas, the lesions ulcerate and rather marked scab formation takes place. This heals in about two weeks, leaving no scar.

Artificial pupils have been burned in several rabbit eyes (fig. 12-A and B), but, so far, we have only attempted to burn two human cases, both aphakic eyes. In one of these the contact cooling chamber was employed and instead of burning the iris as was expected, coagulation of the cornea occurred. This was apparently due to the rather critical focus as a result of using the cooling chamber and the beam was inadvertently focused more on the cornea than on the iris.

It must be kept in mind, if iris lesions are to be burned in the nonaphakic eye, spot coagulation of the lens takes place beneath the pigmented iris lesion. If this is far out in the periphery, it will apparently occasion no difficulty. Therefore, if such a lesion is to be treated with the light coagulator, the pupil should be widely dilated, or a central or paracentral coagulation of the lens may result with some loss of visual acuity.

SUMMARY AND CONCLUSION

From our experience with light coagulation, it is our belief that this therapeutic tool is a valuable addition to the armamentarium of the ophthalmologist. Its full potentialities are yet to be realized. Already, however, it is apparent that such therapy is the method of choice in treating certain lesions. No retinal detachment service can afford to be without a light coagulator.

The importance of predetachment symptoms, such as light flashes and sudden showers of vitreous opacities, must be publicized in order that simple prophylactic light coagulation can be carried out early, before true detachment occurs, necessitating surgical intervention.

2015 Monument Avenue (20).

REFERENCES

1. Guerry, D., III, et al.: Experimental production of flash burns in the rabbit retina. Tr. Am. Ophth. Soc., **54**:259, 1956.

2. Ham, W. T., Jr., et al.: Flash burns in the rabbit retina: As a means of evaluating the retinal hazard from nuclear weapons. Am. J. Ophth., **46**:700 (Nov.) 1958.

3. Guerry, D., III, et al.: Photocoagulation of the retina: Report of a successfully treated case of angiomatosis retinae. Am. J. Ophth., **46**:463 (Oct.) 1958.
4. Meyer-Schwickerath, G.: Licht Koagulation, eine Methode zur Behandlung und Verhuetung der Netzhautabloesung. XVII Conc. Ophth., 1954, **1**:404, 1955.
5. ———: Licht Koagulation. Arch. f. Ophth., **156**:2, 1954.
6. ———: Prophylactic treatment of retinal detachment by light coagulation. Tr. Ophth. Soc., 1956.
7. ———: La photo-coagulation du fond d'oeil et de l'iris. Ann. d'Ocul., **39**:6, 1956.
8. ———: Licht Koagulation von choroidolen melanomen. Tr. XVIII Internat. Congress Ophth., 1958.
9. ———: Licht Koagulation in der prophylaxe der Netzhautabloesung. Discussion at XVIII Internat. Congress Ophth., 1958.
10. MacLean, A.: Hemangioma of the choroid. Alumni meeting, Wilmer Institute, Baltimore, March, 1959.

BRONCHOGENIC CARCINOMA*

With metastasis to aphakic eye

Frank E. Fishof, M.D.
Wilkes-Barre, Pennsylvania

Following is a report of a case with a rare ocular finding.

Case report

On February 24, 1956, a white man, World War I veteran, aged 61 years, a railroad fireman by vocation, who for the last 25 years had not been working because of "arthritis in the legs," was hospitalized for treatment of progressive loss of vision in the left eye of about three years' duration. He was seen by an ophthalmologist who recommended hospitalization for cataract therapy.

Past history disclosed that he had developed deformity of his lower extremities during childhood. His mother died of cancer of the stomach and a brother died of cancer of the lung.

Physical examination displayed an obese individual weighing 200 pounds, whose voice was characteristic of a chronic laryngitis and who had a waddling gait. He did not appear acutely ill. Breathing was of the mild emphysematous type. He frequently cleared his throat. Chest expansion was poor. There were few moist rales which disappeared on coughing. Cardiovascular system was not remarkable. Blood pressure: 154/70 mm. Hg.

External appearance of the eyes was not significant. Pupils reacted to light and accommodation and to consensual reflexes. No abnormal tension was found as judged by finger palpation. Visual acuity in the right eye was 20/70, corrected to 20/20 using +0.5D. sph. ⊃ +1.5D. cyl. ax. 70°

Ophthalmoscopy revealed a brownish, thin-veiled opacity within the cortex of the lens. Details of the vitreous and fundus were discernible. The optic disc was clearly delineated. Visual acuity in the left eye was limited to 15/400, not correctible. Cornea, anterior chamber, and filtration angle did not display abnormalities. The lens presented a veiled opacity of advanced stage involving the cortex. Details of the fundus could not be seen except for a red light reflex.

Hemogram, serology, and urinalysis were within normal range. X-ray studies (fig. 1) of the chest on February 27, 1956, were reported as showing "occasional nodular changes throughout the pulmonary fields, most marked on the right side and upper lung region. There is beginning conglomerate changes in the right upper lobe region. The findings are consistent with second to third stage anthracosilicosis."

Cataract extraction (extracapsular) of the left eye was performed on March 5, 1956. Vision obtained was 20/30 with aphakic correction.

On May 14, 1957, the patient was readmitted for removal of cataract of the right eye. The lens had undergone complete cataractous metamorphosis. Vision dropped from 20/20 to 20/200. The left eye displayed a thickened postcataract extraction capsule partly off center of vision. With aphakic correction, vision remained 20/30. However, the patient had to place his head in position to get optimum vision. Ophthalmoscopically the retina, as well as the uvea, showed no pathologic finding. Capsulotomy was contemplated after operation on the fellow eye. X-ray studies (fig. 2) of the chest disclosed a very significant change in the right lung, as compared with the picture taken on his first admission. It revealed a shadow interpreted to be a "pneumonic consolidation involving the right upper lobe." The temperature was

* From the Eye-Ear-Nose-Throat Section, Surgical Service, Veterans Administration Hospital.

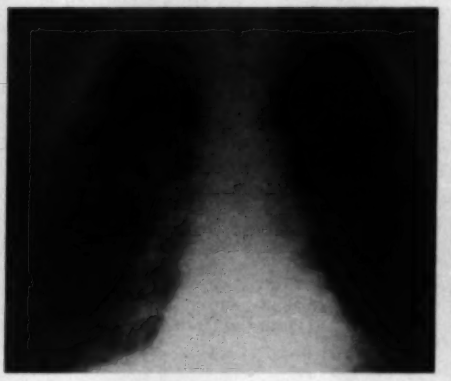


Fig. 1 (Fishof). Roentgenogram on first admission (February 27, 1956) for cataract surgery on the left eye. Note nodular changes right side upper lung fields "consistent with second to third stage anthracosilicosis."

at no time above normal. He did not complain of unusual discomfort in the chest, nor was his coughing more extensive. As far as the patient was concerned, he felt better because of the loss in weight. On May 24th, under local anesthesia, cataract of the right eye was successfully removed. Vision obtained was 20/25, using +10D. sph. for correction.

On November 1, 1957, patient presented himself at the Eye Clinic complaining of poor appetite, weakness, loss of weight, and headaches more pronounced in the region of the left eye. He had the

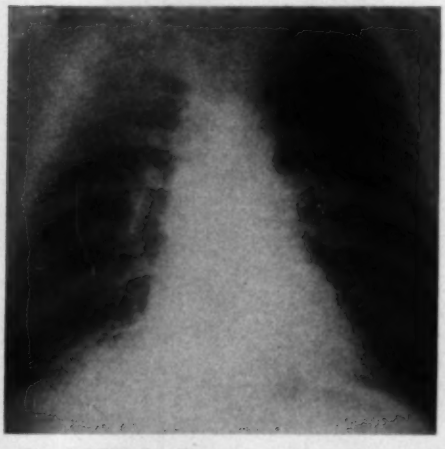


Fig. 2 (Fishof). Roentgenogram on second admission (May 14, 1957) for cataract surgery on right eye. Note shadow interpreted as "a pneumonic consolidation involving right upper lobe."

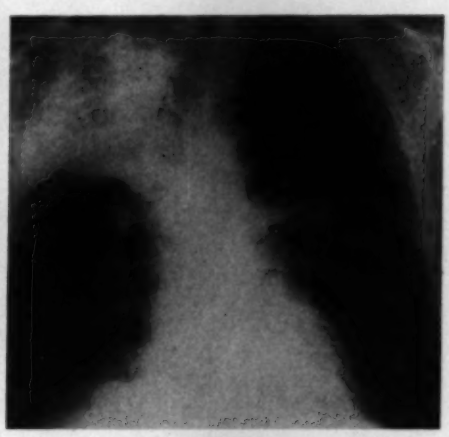


Fig. 3 (Fishof). Roentgenogram on third and final hospitalization (November 1, 1957). Note homogenous clouding and elevation of horizontal fissure. Roentgenologist stated "bronchogenic carcinoma of right upper lobe should be entertained."

appearance of a nontoxic individual whose general health was rapidly failing.

Vision in the left eye was 20/40 with aphakic correction. The conjunctiva and the anterior and posterior segments, as viewed with the ophthalmoscope and slitlamp, did not show any appreciable pathologic process other than that residual to cataract surgery. There was no impairment in mobility of the eye in its cardinal directions. Tension was normal to finger palpation. Vision in right eye was 20/25 with correction and was otherwise not remarkable. He was referred for admission to the Medical Service.

Chest X-ray films (fig. 3) taken the same day were reported as follows:

"Compared with the previous film (May 14, 1957) this shows that the right upper lobe has a dense homogenous clouding and some elevation of the horizontal fissure. Bronchogenic caricinoma of the right upper lobe should be entertained."

Bronchoscopy (November 11, 1957) showed an overgrowth of tissue in the right main bronchus in the region of the upper lobe orifice. Tissue study of the biopsy growth was interpreted to be "squamous-cell carcinoma of right bronchus." Bronchial fluid aspirations were graded Class V cells, conclusive for malignancy.

Fig. 4 (Fishof). Neoplastic eye 13 days prior to enucleation.

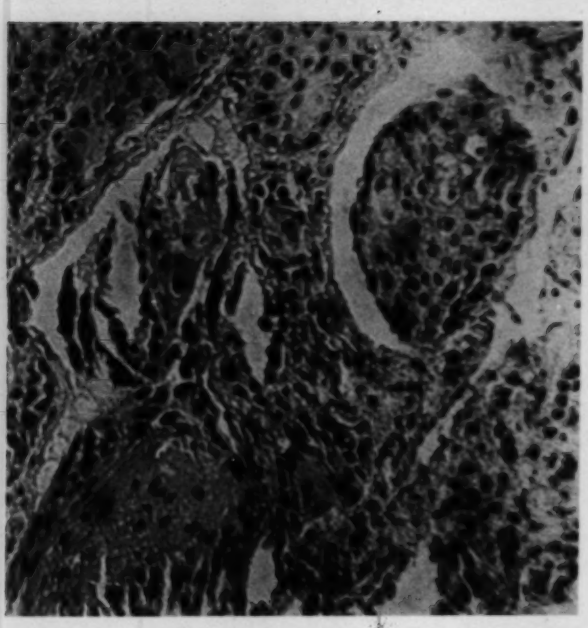


Fig. 5a (Fishof). Section of biopsy of episcleral tumor, squamous-cell carcinoma.

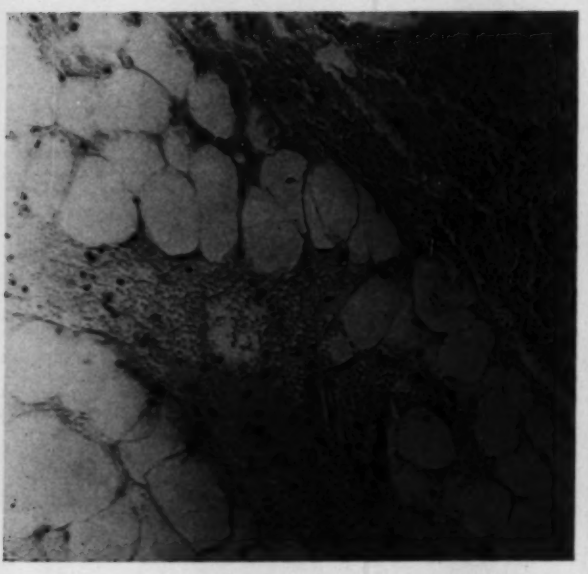


Fig. 5b (Fishof). Periorbital tissue free of neoplasm.

The day after bronchoscopy, patient was examined at the Eye Clinic, at which time a hard subconjunctival mass which was raised above the normal surface of the left eyeball was noted. It extended from the 9- to 12-o'clock position and was limited anteriorly by the limbus. Its maximum elevation was at the vertical axis. The conjunctiva covering the growth was a dark waxy hue. It was not tender.

Vision with glasses was 10/400. Ocular tension was 16.9 mm. Hg in the affected left eye and 23 mm. Hg (Shiøtz) in the right eye. Vision in the right eye was 20/25 with glasses, and objectively and subjectively, this eye was not affected.

The neoplasm (fig. 4) continued to increase circumferentially. On December 4th, it extended along the entire nasal half of the eyeball between the equator and the limbus. There was absolute loss of vision. Mobility was not affected. The anterior chamber appeared blocked on the nasal half. The fundus could not be seen. Within a few days, the eyeball prolapsed and the patient began to feel uncomfortable.

Biopsy (figs. 5a and 5b) of the noninflammatory mass, taken at its maximum elevation, was reported squamous-cell carcinoma. The eye (figs. 6a and 6b) was enucleated on December 18th, about seven weeks after hospitalization. At that time the growth extended along the entire circumference of the limbus except for the arc between the 4- and 6-o'clock position. It did not cross the limbus anteriorly. The specimen was sent to the Armed Forces Institute of Pathology for diagnosis.

The general condition of the patient deteriorated rapidly. He died January 21, 1958, 31 days after enucleation; 81 days after his last hospitalization; and seven months and seven days after roentgenograms revealed "pneumonic consolidation involving the right upper lobe."

Fig. 6a (Fishof). Enucleated eyeball, front view.

Fig. 6b (Fishof). Enucleated eyeball, superior view. Note nodular seedlings behind the equator and anterior to the nerve.

AUTOPSY FINDINGS

A. GROSS

The right lung (fig. 7) presented a thick pleura at the apex, a gross tumor confined to

Fig. 7 (Fishof). Lungs. Bronchogenic growth extending to upper lobe bronchus. Tumor replacing upper lobe parenchyma. Primary site of growth.

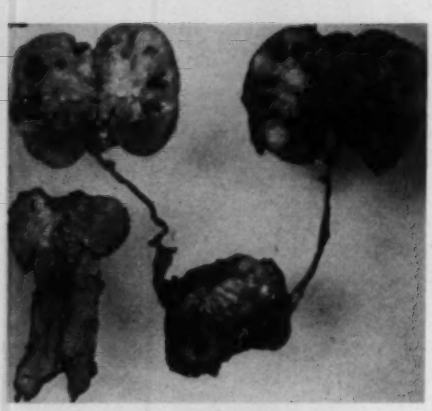


Fig. 8 (Fishof). Kidneys (tumor tissue infiltrating parenchyma) and pancreas (tumor invading parenchyma).

the upper lobe with necrosis in its center, and an emphysematous bleb the size of a hen's egg. Gray-white tissue that partly filled the main stem bronchus extended into the bronchus of the upper lobe. The middle and lower lobes showed diffuse bronchopneumonia. The left lung was essentially negative except for anthracosilicosis and suggestive pneumonia of the lower lobe. The parenchyma of the left adrenal and both kidneys (fig. 8) was infiltrated with gray-white tumor tissue. The pancreas (fig. 8) and paraaortic (fig. 9) lymph nodes were also invaded. The sigmoid displayed a hard mass, the size of a "pullet's egg." At the point where it bulged into the mucosa there was an ulcer. The brain was not involved.

B. Microscopic

The tissue of the lungs (fig. 10) displays many tumor giant cells, bizarre mitosis, and ephithelial pearls. In some places the growth is diffuse and free of pearls. In the lymph nodes the tumor is growing in solid cords of anaplastic cells. Pearls and giant cells are not present. The tumor pattern in the kidney is essentially the same as in the lung, except for the added focal collections of chronic inflammatory cells located chiefly in the cortex.

Report on eye (A.F.I.P. accession #846785)

A. Gross (fig. 6)

The salient findings are:

1. A firm, tan-white, cartilaginous, nodular growth around the nasal limbus from the 5:30 to 12-o'clock position. The mass averages 7.0 mm. in thickness.

2. There are three tan-white nodular masses behind the equator and 5.0 mm. anterior to the nerve.

3. The globe transilluminates well except for a small area between the nerve and the nodule near the equator.

4. The ciliary body, the anterior choroid, and equatorial sclera at the 11-o'clock position are infiltrated with tumor. The posterior choroid is infiltrated to a lesser degree.

5. Numerous focal areas of retinal detachment.

6. Nervehead is slightly edematous.

Fig. 9 (Fishof). Abdominal aorta and paraaortic lymph nodes. Nodes are loaded with metastatic neoplasm.

Fig. 10a (Fishof). Lungs. Histopathology of primary site of metastases. Squamous-cell carcinoma and anthracosilicosis.

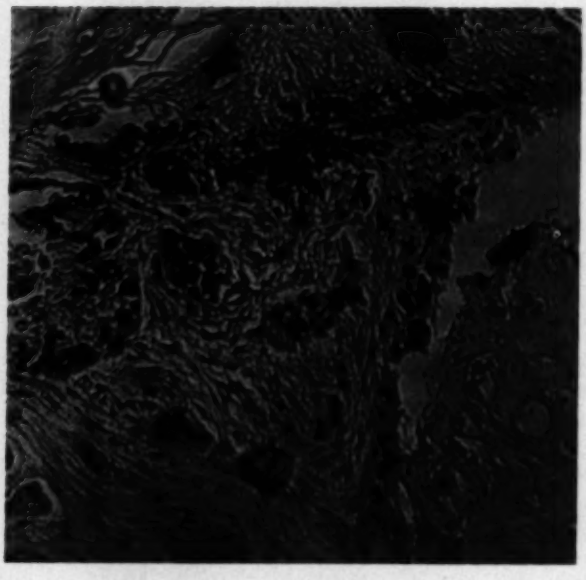


Fig. 10b (Fishof). Lungs. Squamous-cell carcinoma in the bronchus spreading to pulmonary parenchyma.

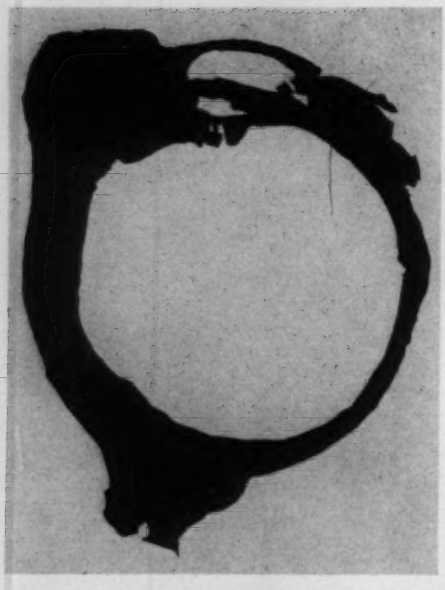


Fig. 11 (Fishof). Cross section of eye by A.F.I.P. (accession #846785). Note tumor on nasal side extending into anterior chamber along post-operative sclerocorneal scar.

B. Microscopic (fig. 11—Cross section)

1. The large epibulbar mass is composed of strands of anaplastic malignant cells showing little tendency toward keratin formation.

2. Extension of the tumor (figs. 12a and 12b) along the corneal scar into the anterior chamber and on the anterior iris surface.

3. Ciliary body infiltrated by tumor to a varying degree. Some sections completely replaced by tumor. Large areas of necrosis noted.

4. The retina is generally free of invasion but in the immediate peripapillary region some sections show beginning infiltration of the retina by small nodules of tumor.

5. The choroid is infiltrated with tumor and shows extensive areas of necrosis.

6. The sclera shows invasion superiorly both externally and from the choroid.

7. Edema of the peripapillary region continues with the edema of the nervehead.

8. The sheath of the optic nerve and the fibrous tissue adjacent to the sheath is generously loaded with tumor cells.

9. The nerve itself appears to be free of invasion.

C. Diagnosis

Squamous-cell carinoma, metastatic to the eye from bronchus with involvement of the subconjunctiva, episclera, ciliary body, choroid, and "epithelization" of the anterior chamber by tumor.

Summary

1. A white man, aged 61 years whose mother died of cancer of the stomach and brother died of cancer of the lung, had cataract extraction of the left eye on March 5, 1956. About 15 months later, extracapsular cataract extraction of the fellow eye was performed. Vision obtained in each eye was satisfactory.

2. Roentgenograms on first admission displayed conglomerate changes in the right upper lobe "consistent with second to third stage anthracosilicosis." On second admission, the right upper lobe revealed "a pneumonic consolidation." No change in vision in the left eye was found.

3. On November 1, 1957 (about 20 months after first admission), chest X-ray studies disclosed right upper lobe consolidation suggestive of bronchogenic carcinoma. Bronchoscopy confirmed impression. No pathologic condition of the eyes suggestive of neoplasm, extraocular nor intraocular, as viewed with ophthalmoscope and slitlamp, was noted.

4. About three weeks after the third admission, a small episcleral nodular growth appeared on the left eye. Vision dropped from 20/40 to 10/400. The tumor rapidly spread along the nasal side of the eye and invaded the interior along the sclerocorneal surgical incision. Biopsy of episcleral growth was reported "squamous-cell carcinoma."

5. The Armed Forces Institute of Pathology (accession #846785) diagnosed the

Fig. 12a (Fishof). Sclerocorneal region, temporal side. Free of neoplasm.

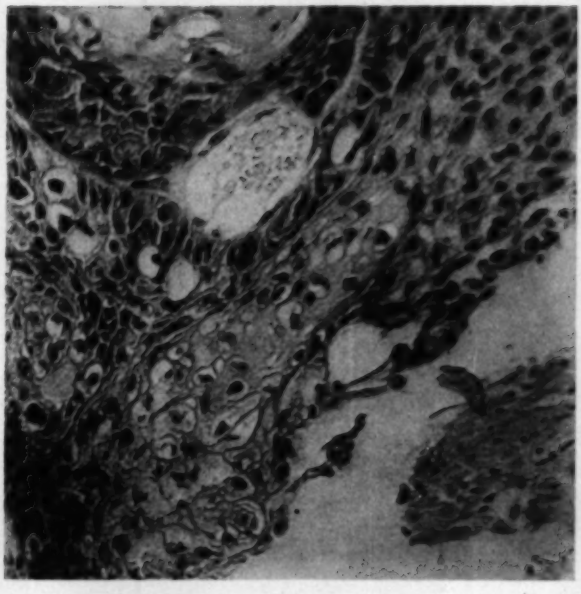


Fig. 12b (Fishof). Sclerocorneal region, nasal side. Anaplastic tumor cells wildly disseminating.

enucleated eye "squamous-cell carcinoma, metastatic to the eye from bronchus with involvement of the subconjunctiva, episclera, sclera, ciliary body, choroid and 'epithelization' of anterior chamber by tumor."

6. Autopsy uncovered a gross solid tumor confined to the right upper lobe with necrosis in its center. Cancerous tissue occupied the right main stem bronchus. There was metastasis to both kidneys, left adrenal, pancreas, sigmoid and para-aortic lymph nodes. Microscopy confirmed the gross impression of bronchogenic carcinoma with metastasis.

7. The patient died seven months and seven days after the roentgenograms disclosed a "pneumonic consolidation involving the right upper lobe," which proved to be bronchogenic carcinoma that metastasized to the aphakic eye and abdominal viscera.

Veterans Administration Hospital.

ACKNOWLEDGMENTS

I am grateful to Dr. Anthony J. Kameen, attending consultant ophthalmologist, for his valuable assistance, and to Dr. George J. Brilmyer for his special interest in evaluating the necropsy and microscopic findings. Thanks are extended to the Armed Forces Institute of Pathology for reporting the macroscopic and microscopic condition of the enucleated eye. The co-operation of the librarians, Miss L. A. Geroulo, Miss B. J. Stathakis, and the medical photographer, Mr. A. Andreeko, is greatly appreciated.

THE PATHOGENESIS AND PATHOLOGY OF OCULAR ONCHOCERCIASIS

PART I. INTRODUCTION TO THE SUBJECT AND THE THESIS

F. C. RODGER,* M.D., M.CHIR.
Oxford, England

This thesis will describe the results of my investigations into the pathogenesis and pathology of ocular onchocerciasis in the interior of Africa during the period 1952 to 1956. In British territory this disease has only begun to be recognized since the last war. Now it is appreciated that the problem it presents is of the highest importance to those regions where its ravages occur, an area which embraces the greater part of the African Continent. The northern limit is defined by the Sahara, because of lack of water and the arid atmosphere; the southern limit reaches into Angola in the west and the upper reaches of the Limpopo in the east. I have had the opportunity of studying the disease in several selected areas between the Congo rapids and the River Niger, as far north as Timbuctoo, and westward toward the Gulf of Guinea. For the greater part the work was carried out in Ghana, Nigeria and the Cameroons.

It is an indication of the size of the problem that Stoll, in 1947, estimated that 19 million people in Africa were suffering from onchocerciasis; in 1957, my estimate was double that number. There may be no less than a half-million Africans blinded by this disease alone. In the territories in which I worked (in Commonwealth or British Colonial or Mandate territory) there are approximately 350,000 blind from all causes; of these perhaps 20 percent have been blinded by onchocerciasis, or, as it has come to be known, "river blindness." This figure is high because the areas were for the greater part heavily endemic. The worst area of all was in North Ghana, where in a population of one million, we estimated that 600,000 people suffered from the disease, and 18,000 had been blinded by it. This should make the magnitude of the problem quite clear.

* From the Visual Research Unit, Oxford University.

Onchocerciasis is a disease which results from the infestation of man by a filarial worm, Onchocerca volvulus Leuckart. In 1893, Leuckhart was sent samples extracted from subcutaneous nodules excised in the Gold Coast (as Ghana was then called) by an unnamed German missionory. The worm was called Filaria volvulus. It is interesting to note, nevertheless, that nearly 20 years before, in 1874, John O'Neill, an Irish surgeon on board H.M.S. Decoy, a frigate stationed off Cape Coast in Ghana, examined a piece of skin taken from a patient sent from the Addah Fort Hospital at the mouth of the Volta, and recognized the presence of microfilariae (mf.) in the dermis under the microscope. There is little difficulty in identifying them as mf. volvulus from the drawings in the Lancet of 1875.

Following Leuckart's description, however, it was the nodules with their contained adult worms that attracted attention. Brumpt (1904) suggested Glossines and Simuliidae might be the cause of the nodules, and thus hit the target first time. In 1910, Railliet and Henry classified all the Onchocerca filariae, describing the species' characteristics; among them appeared Leuckart's Filaria volvulus, given its full name for the first time.

It was not until 1915 (publishing being delayed until 1919 because of the Great War) that the worm was discovered in the Americas by Robles. Brumpt (1919) believed this to be a new species which he called O. caecutiens (literally the "blinding filaria"), an excellent choice of name based on the fact that Robles had been the first to associate blindness with the disease; he had even suggested two species of Simuliidae as vectors; this species of Onchocerca, however, turned out later to be identical with volvulus.

Pacheco-Luna (1920) was the ophthalmic surgeon called in by Robles to investigate the ocular manifestations of the anterior segment in detail—just as he had called in Brumpt as a leading helminthologist to iden-

Frontispiece (Rodger). Ocular onchocerciasis. Three blind men in the town of Nakong in North Ghana. One is also suffering from leprosy.

tify the worm. The aged Pacheco-Luna may be seen today sitting in hisParis garden puffing at his pipe, the last survivor of these South American pioneers.

It is amazing to think that in Africa, where the worm had first been identified long before and where several million people were suffering from the disease, it was not until 12 years after Robles' pronouncements that Hissette (1931, 1932), a Belgian, showed that O. volvulus was an even greater cause of blindness in Africa than in Central America.

The first British worker on the scene was the Scot, Bryant (1935), who, in describing a posterior segmental lesion to Hissette when they met on furlough, was advised to look for mf. volvulus, for although Hissette at that time had not published any description of the chorioretinal changes, he had observed them, and suspected the diagnosis. Bryant promptly discovered onchocerciasis in the Sudan, and generously acknowledged the tip he had received from Hissette. He will always be known as the first to publish a description of the posterior condition. Meanwhile, in Sierra Leone, another British worker was carrying man's knowledge of this strange disease further. Blacklock (1926a,b, 1927) was the first to demonstrate that S. damnosum Theobald was the vector of the larval stage of O. volvulus in Africa. The descriptive terminology given this species of Simuliidae is a particularly happy one, so irritating is its bite. Hissette (1932) found that S. neavei Roubaud was a carrier in Central and East Africa, and Becquaert (1934) later identified three vectors in Central America, S. Metallicum Bellardi, S. ochraceum Walker, and S. mooseri Dampf; the first is the most prolific vector. At the moment no other vector has definitely been recognized, as far as I know, although many have been sought.

Hughes (1949) suggests that while European doctors were laboriously piecing together the picture of onchocerciasis, the bush Africans in the endemic areas had formed a fairly accurate idea. Saunders (1929) mentions that in the Gold Coast of his day nodules on the head were associated with blindness by the Lobi-Dagartis. Dry (1921) found that in Kenya blindness and skin irritation were both claimed to be caused by the bite of black flies. Buckley (1949) learned that the inhabitants of an infected village in the Congo also associated blindness with biting flies. Waddy (1951), in Ghana, speaks about a chief who blamed the nodules for all ills, including sterility. With his usual dry wit, Waddy remarks of this man that despite an ample stock of worms he had managed to procreate 20 children! Maybe it is a bit too ingenuous of Hughes to praise the perspicacity of the bush-dwellers; my own experience was that the mass of people were ignorant of the cause and, indeed, even of the fact that the incidence of blindness among them was at all unusual.

After Pacheco-Luna's observations of 1920 several reports in Spanish on the relation of onchocerciasis to blindness were published in Central American journals. They did little to advance our knowledge of the condition, judging by the English summaries. The latter, of course, are often incomplete or incomprehensible. In Africa, after Hissette's exciting new observations, Strong and his Harvard team, who had been studying in Mexico and Guatemala, joined the Belgian in the Congo; no ophthalmic surgeon had ever worked with Strong previously. As a result of their collaboration, a combined monograph appeared in 1938. In this book, Hissette merely repeated his early observation.

No further interest by British workers in Africa appears to have been taken until Ridley (1945) spent a fortnight, during his war service in West Africa, in North Ghana studying the ocular manifestations. His highly competent and comprehensive monograph is at present the standard work in our own literature. It is remarkable considering the short time he had at his disposal, but then he was the first highly skilled modern ophthalmic surgeon to study onchocerciasis. This work resulted in a spate of activity among other British workers, myself included. In this regard, Wilson, Director of

the Royal Commonwealth Society for the Blind, and a member of the Royal Commission into Blindness in the Colonies (1948), was the driving force which led to my West African Ophthalmic Survey. A blind man himself, Wilson tramped all over West Africa asking questions. His conclusions have proved basically correct but caused quite a furore at the time.

Despite the long start in Central America, up to 1930 nobody had reported on the pathology of the condition. Ochoterena (1927), in a paper purporting to cover the pathology of onchocerciasis, does not mention the eyes (1927). It was another three years before he obtained his first eyeball, quickly followed by two others (1930). These eyes were excised after death. Although, in the light of modern pathology, they appear somewhat superficial, these papers were a start. Microfilariae were found in all tissues except the retina and optic nerve.

It was Strong, working in Central America, who produced the first really sound paper, describing the association of the parasites in the eye with lesions of the conjunctiva, cornea and iris. This was published in 1934, just before Bryant described the posterior changes. Strong's observations were drawn from two eyeballs and 11 pieces of biopsy tissue.

Hissette, in his early papers, discussed the pathology including the presence of mf., although no mention is made of them in the text. It is left to the reader to draw his own conclusions from the excellent photomicrographs, which showed the parasites in the conjunctiva, cornea, iris and choroid. Hissette does not mention from how many eyes or biopsies he drew his conclusions. It seems to have been one only. The Belgian gives the impression of being a man of great imagination and talent, who unfortunately expresses himself badly in words. In the same year Giaquinto (Mira) reported finding mf. volvulus in the optic nerve. Up to 1934, therefore, apparently there had only been six or seven eyeballs examined, along with an unknown number of biopsy examinations.

Bryant of the British workers first presented pathologic observations, somewhat briefly in his paper and rather more fully in a thesis (1935a,b). He told me that two eyes were sectioned, eight others being stored in a building subsequently blown up in the blitz. He purchased his material. Hughes obtained one eye at autopsy, which was the basis of his Oxford thesis. He remarked on the difficulty of persuading the African to undergo a surgical operation of this nature. Ridley also remarked on the difficulty of getting eyes; he was unlucky and got none.

As no other reference can be found in the literature, it would seem that at a reasonable estimate the pathology of the ocular lesions of onchocerciasis is based on studies from about 10 or 12 eyes (three by British workers) and a large number of biopsies. I can count myself fortunate to have obtained by persuasion 20 selected eyeballs and 80 pieces of biopsy tissue; all together every stage of every lesion is covered. Although a little of the material was subsequently discarded for various reasons which will be given later, there was still enough to provide ample scope for a comprehensive report. The eyes were excised under general anesthesia, in the bush; biopsies involving keratoplasty, sclerectomy, and iridectomy were carried out under local anesthesia. The background to this surgery has been written up elsewhere (Rodger, 1958).

The pathogenesis of the ocular manifestations has generally been considered dependent upon the death of the microfilariae in the affected structure. Early workers, like Robles (1919) and Calderon (1920), were inclined to believe that the eye symptoms were due to a toxin secreted by the adult worms. It was Strong (1934), who first declared emphatically that it was the microfilariae which led to the tissue reactions. The fact is this was only a hypothesis, based on circumstantial evidence, which is frequently a misleading premise in medicine and surgery. What is remarkable is the lack of interest in the microfilariae in the early Central Ameri-

can papers; O'Neill's observations in the Lancet went unnoticed for 50 years. Strong's views, therefore, were in a way revolutionary at the time. He was equally emphatic that the ocular manifestations were chronic in nature, citing his pathologic material as evidence of this fact. As Hissette held the same views, and as these two men stood above most of their contemporaries, it is not surprising this opinion has held sway ever since. It may be that workers in the 1930s were handicapped by the lack of pathologic material, none of which afforded evidence of an acute lesion.

It is not easy to explain, nevertheless, why nobody except me has ever reported seeing the acute phase, short though the duration of the attack may be. I have carried out iridectomies in several acute anterior uveitis cases and found the iris tissue filled with the motile parasites. I have viewed microfilariae in the cornea with the slitlamp in eyes that were so photophobic the lids had to be held forcibly apart. In the course of investigating treatment, many dozens of acute onchocercal eyes were handled, thereby refuting part of Strong's opinions. Fortune no doubt played a part in first sending the team which I led to what is perhaps the most heavily infested area in the whole world. Later, in other parts of the African interior, we went many months without seeing an acutely infected eye. The importance of all this lies in stressing the vacuum which existed before the war in our knowledge of the disease, not only in regard to the pathogenesis and pathology but even the symptomatology.

Although the exotoxin theory was generally abandoned in favor of Strong's final arguments that it was the dead bodies of the microfilariae which caused the inflammation, it did not necessarily mean that he was right.* There may be other factors. Rodhain (1949) is convinced that allergy plays a part, and Toulant (1953) supports this view, believing that a hypersensitive state is responsible for some of the ocular lesions, if not all. This, he claims, is why only some subjects are affected. These three possibilities exist, undoubtedly: a direct toxic effect resulting from the products of disintegration of the microfilariae bodies, a circulating exotoxin emanating from adults or microfilariae, or the induction of a hypersensitive state with which is bound the question of antibody formation. None of these a priori hypotheses can be ruled out, for they have neither been demonstrated experimentally, nor disproved. It is believed that this thesis advances our knowledge in this direction.

In the dissertation which follows a series of investigations into the problems posed above will be described. Three approaches to the subject have been taken: in Parts II and III the pathogenesis is discussed, largely in the light of animal experiments, based on a technique we evolved to isolate the microfilariae when alive; in Part IV the microscopic appearances of the various ocular lesions are given, each description being prefaced by the salient clinical and macroscopic features; finally, in Part V the threads are briefly drawn together.

Numerical references are given at the end of each Part, except in the case of Part I, this introduction, where references are given by dates, a system that seems to be better suited to a chronologic review of this kind. Photomicrographs are not referred to in the text, for I find this much less instructive than the method of placing them at the end in the form of an Appendix, where the story may be followed in pictures.

* Strong made several other suggestions before fixing finally on the theory that it was the disintegrating bodies of the microfilariae which caused the trouble.

Bibliography

1875: O'Neill, J.: Lancet, 1:265. (Discovered and drew what was subsequently found to be mf. volvulus in skin biopsy in Ghana.)

1893: Leuckart, R.: (The only reference found being in Manson's chapter on skin diseases in Davidson's *Textbook of Tropical Hygiene and Disease in Warm Climates*. First named the adult "Filaria volvulus"; obtained in nodule sent from Ghana.)

1904: Brumpt, E.: Rev. Med. & Hyg. Trop., **1**:43. (Suggested vector of F. volvulus to be Glossines or Simuliidae.)

1910: Railliet, A., and Henry, A.: Comp. rend. Soc. Biol., **68**:248. (Classified Filaria volvulus Leuckart as a species of Onchocerca.)

1919: Brumpt, E.: Bull. Soc. Path. Exot., **12**:464. (Described O. caecutiens as new species of Onchocerca in Central America, the specimens being supplied by Robles. It is identical with O. volvulus.)

1919: Robles, R.: Bull. Soc. Path. Exot., **12**:442. (Discoverer of ocular onchocerciasis and its relation to Filaria Onchocerca, classified incorrectly by Brumpt as a different species from O. volvulus. Also claimed Simuliidae were vectors.)

1920: Pacheco-Luna, R.: Rev. Cubana Oft., **80**(Reprint series), pp. 20. (First ophthalmic surgeon to describe ocular onchocerciasis, co-operating with Robles.)

1920. Calderon, V.: Tesis inaugural, Tip. Sanch. Guise, Guatemala, pp. 107. (Reviewed condition and made suggestion that lesions were caused by exotoxin from adults.)

1921: Dry, F. W.: Bull. Eng. Res., **12**:233. (Noted association of blindness in Africa with biting flies.)

1926a: Blacklock, D. B.: Ann. Trop. Med. Parasit., **20**:1. (First to infect S. damnosum with mf. volvulus from man.)

1926b: ———: Ann. Trop. Med. Parasit., **20**:203. (First to observe development of infective larval stages in fly.)

1927: ———: Brit. M. J., **1**:129. (Suggestions as to aetiology of nodules.)

1927: Ochoterena, I.: Rev. Mex. Biol., **7**(3):55. (First to describe pathology of nodules.)

1929: Saunders, G. F. T.: Ann. Rep. Med. San., Gold Coast, p. 126. (Association of blindness by natives with nodules on their bodies reported.)

1930: Ochoterena, I.: Rev. Mex. Biol., **10**:75. (Pathologic observations on the first human eyes infected with mf. volvulus. Describes presence of mf. in cornea, iris and choroid.)

1931: Hissette, J.: Ann. Soc. Belge Med. Trop., **11**:45. (First report of blindness due to onchocerciasis in Africa, and S. neavei as vector in Central and East Africa.)

1932: ———: Ann. Soc. Belge Med. Trop., **12**:433. (Full description of ocular lesions, and report of finding mf. in cornea, iris and choroid. Suggested a choroiditis might occur.)

1934: Giaquinto (Mira), M.: Rif. med., **50**:858. (Observed mf. volvulus in optic nerve for first time.)

1934: Strong, R. P.: Onchocerciasis. Cambridge, Mass., Harvard Univ. Press, Part VIII, p. 78. (Pathology of anterior segment with mf. observed in cornea and iris. First suggestion that it was *dead* mf. which caused the lesion.)

1934: Becquaert, J. C.: Cambridge, Mass., Harvard Univ. Press, Part IX, p. 91. (Discovered three species of Simuliidae that act as vectors in Central America.)

1935a: Bryant, J.: Tr. Roy. Soc. trop. Med. & Hyg., **28**(5):523. (First to describe retinal-choroiditis in posterior segment and associate it with presence of O. volvulus in Sudan.)

1935b: ———: Thesis, Edinburgh University. (Pathology of posterior lesion in two eyes.)

1938: Hissette, J.: Am. J. Trop. Med., **18** (Suppl.) Part II, p. 58. (Repetition of his earlier work in English.)

1945: Ridley, H.: Brit. J. Ophth., Suppl. X. (Review of entire subject with original observations of mf. in cornea as viewed with slitlamp, and clear description of posterior lesion, which differed from Bryant's description.)

1947: Stoll, N. R.: J. Parasit., **33**:1. (Estimate of total African population infected as 19 million.)

1948: Wilson, J. F.: Blindness in British and Middle East Territories. London, H.M. Stationery Office. (The report of a Joint Committee appointed by the Colonial Office and the Royal National Institute for the Blind, following the visit of a Delegation to Africa and certain Middle East Territories between July, 1946 and March, 1947. This emphasized the high incidence of blindness.)

1949: Buckley, J. J. C.: J. Helminth., **23**:1. (Blindness associated with black flies by Africans in Congo.)

1949: Hughes, M. H.: Thesis, Oxford University. (Comprehensive review with detailed pathology of one eye showing mf. in cornea, iris, and at inner edge of sclera.)

1949: Rodhain, J.: Ann. Soc. Belge Med. Trop., **29**:177. (Discussion of all filarial types including volvulus, and possibility of allergic reactions.)

1951: Waddy, B. B.: Onchocerciasis and blindness. D.M.S. Rep., Gold Coast, pp. 36. (Report of field survey which produced evidence that the disease was the greatest cause of blindness there is in Ghana. Mentioned possibility of a concomitant vitamin deficiency affecting the disease.)

1953: Toulant, P.: WHO unpublished report at the first meeting in Mexico of the Expert Committee on Onchocerciasis. (Based on many clinical papers, reviewed disease and its possible pathogenesis, suggesting a hypersensitive state determined the onset in certain subjects only.)

1958: Rodger, F. C.: Blindness in West Africa, Part II. London, H. K. Lewis, 1959. (Clinical and statistical results of four-year survey in West Africa. First to discover mf. volvulus in retina; demonstrated the parasites in every ocular tissue including the ciliary body, vitreous, and optic nerve. Suggested two types of posterior lesion existed. Reported lesions sometimes had short acute phase.)

Part II: The pathogenesis

Introduction

Apart from my preliminary paper (Rodger[1]), there has been no attempt to investigate the pathogenesis of the ocular lesions experimentally. Early workers were more interested in the hypersensitivity of the skin which occurs as a result of the death of the microfilariae in man.

Rodhain and Dubois[2] described intradermal reactions which they induced but pointed out that it was a group reaction involving F. loa and W. bancrofti as well as O. volvulus. Toulant[3] and Rodhain[4] believed that hypersensitivity also caused the ocular lesions or at least some of them.

That the skin of man becomes hypersensitive to the parasites seems at first sight likely. The immediate effect of killing massive numbers of microfilariae with diethylcarbamazine is, according to these workers, full evidence of this: pruritis, headache, arthralgia, edema, a transitory eosinophilia, and the fact that antihistamines ameliorate the symptoms, all support the contention. Nevertheless, the early experiments we carried out failed to demonstrate either actively or passively the presence of antibodies in infested human subjects in guinea pig and rabbit skin. A capillary response might have been observed if an intravenous dye had been used; this was not done so one cannot conclude with confidence that an antigen-antibody reaction did not occur. On the other hand the findings might well be correct; there may be a species difference, so that man alone becomes hypersensitive. Whatever we conclude these early experiments were rather disappointing because they proved negative.

Every structure in the eye has revealed inflammation in association with the presence of the parasites in microscopic sections, as have all the ocular lesions except one. The latter, representing only about five percent of all cases of ocular onchocerciasis, is never associated with microfilariae in the posterior segment, and appears to have a different etiology; its pathogenesis will be considered in Part III of this thesis, separately. If O. volvulus is present in 95 percent of the ocular manifestations of onchocerciasis, they are on the other hand frequently also present where no lesion exists. At one time or another various workers have remarked on this finding.

Out of 600,000 people suffering from the disease in North Ghana, of whom roughly one third had parasites within the eyes, only 18,000 had been blinded, and perhaps the same number affected to a lesser degree. High though this figure is, it is surprising it is not much higher. It is difficult to explain why only about one in 20 with microfilariae in the eyes is affected except in terms of a specifically acquired *decreased* sensitivity, or immunity. Inherent in the subject of immunity, of course, is the prospect of there also being in some patients an *increased* sensitivity, as suspected by Rodhain and Toulant.

Sulzberger[5] has defined the dual process of an increase and decrease in sensitivity as one whose component parts are mixed up together, accompanying or following one another in the same tissue or animal, and maybe even resulting from one and the same exposure to the same agent. It would not, therefore, be surprising if the results of any experimental investigation into the pathogenesis of ocular onchocerciasis were to prove contradictory and complex.

The theories around which the experiments now to be described were built can be briefly outlined here. Tests on lower animals, we know, do not necessarily prove the etiologic significance of a suspected human antigen. In passive transfer experiments, nevertheless, to demonstrate the presence of antibodies it is better to use animals rather than humans; the opposite is true in the case of active transfer. At a late stage in the work, we carried out on man some of the procedures earlier per-

formed on animals. This was possible only when we had learned what dosages were safe, and had gained confidence in handling material about which nothing was known but a lot suspected. The problem was approached from three angles:

1. Local tissue hypersensitivity

Although onchocerciasis seems to induce a hypersensitive state in the skin of man, it need not effect the eye in the same way. Using foreign or exogenous antigens an ocular hypersensitivity can be induced, as by egg albumen; if a local tissue hypersensitivity to volvulus protein were to develop in the eye, therefore, it would not be surprising.

Clinically, apart from the fact that the low incidence of ocular crises suggests that the mechanisms of biologic adaptation are at work, there is little with which to support or refute the hypothesis that a local tissue hypersensitivity occurs. The type of ocular lesion found is clinically, on the whole, nonspecific. Only the superficial punctate keratitis is suggestive of allergy (Rodger[6]).

The histopathologic evidence of allergic inflammation, as described in earlier papers, is just as unsatisfactory. It rests entirely on the presence of eosinophil leukocytes, which, as is commonly understood, are to be expected anyway wherever the body is invaded by such parasites. Necrotizing arteritis and focal necrosis, characteristic of a severe tissue allergy, were never seen. The pathology on the whole does nothing to encourage us to believe that the ocular lesions are those of an allergic inflammation.

2. Primary exogenous inflammation

This is the popular theory as to the pathogenesis. Such an inflammation might result from exotoxins secreted by the living adults or microfilariae, or be liberated during the disintegration of their dead bodies. With a well-adapted parasite like volvulus one would not expect the living organisms to cause inflammation, or their pleasant way of life would be upset. There is enough clinical evidence to suggest strongly that the living parasites, both adult and microfilariae, do not induce an inflammatory response. The pathology on the other hand, as first claimed by Strong,[7] indicates it is the dead microfilariae which cause the damage inasmuch as their bodies are seen in the midst of inflammatory cells; there is contradiction here, however, for in the skin, microfilariae have frequently been found unassociated with any inflammatory reaction. The explanation of this probably lies in the fact that Strong *assumed* the microfilariae he observed were dead; in fact no clear-cut picture has been presented which differentiates the living from the dead parasite microscopically, a deficiency which I have made good, as will be shown in Part IV.

3. Primary toxicity inducing either a state of sensitization or of tolerance

Finally, the experiments were planned to allow for the possibility of a substance with a primary toxicity leading either to sensitization or immunity on repeated application. Dinitrochlorbenzene is one such substance, which induces sensitization in guinea pig or man only when applied to the skin in sufficient quantities to produce a toxic reaction. Examples of the opposite state of affairs (inducing tolerance) are every day occurrences. These are possibilities which can only be solved experimentally.

Methods

1. Preparation of a microfilarial suspension

An area of skin found by repeated pinch biopsies to have a large microfilariae population is excised, portion by portion, drawing as little blood as possible, and placed in 25 cc. of Ringer-Locke solution at room temperature for half an hour. Nearly all the microfilariae emerge from the skin during this time, and the pieces of skin and any red blood corpuscles present settle to the bottom. The clear fluid which contains most of the

TABLE 1

RESULTS OF EXPERIMENT 1

a. THE EFFECT OF LIVING MICROFILARIAE ON THE EYE

No. of Microfilariae Injected	Subsequent History of Microfilariae	Structure Involved	No. of Animals	Onset (in hr.)	Effects	Sequelae
10	None seen after first day in 2 animals; doubtfully once or twice owing to flare in third	Anterior chamber and iris	3	48	Slight aqueous flare, cotton-wool exudates at pupil, lasting 3 da.	Total absorption in 2 animals and persistent tag of exudate in 1. Killed at 1, 2 & 3 wk.
12 (repeated once)	One living and one dying mf. seen in same conj. biopsy	Subconj.	3	24–36	Local hyperemia, slight grey opacity of adjacent corneal margin	Complete resolution 2–3 days later. No sequelae. All killed 6 da. after repeat
20	3 motile mf. seen daily for 5 days; a single motile mf. on 12th day; after this doubtful	Anterior chamber	1	120	Transient flare lasting less than 2 da.	No sequelae. Killed after 3 wk.

b. THE EFFECT OF DEAD MICROFILARIAE ON THE EYE

6	Nil	Subconj.	6	2	Severe bulbar hyperemia, then neovasc. of adjacent corneal sector with gray opacity. Chemosis limbus	Resolution started 7th da. and took another wk.
6	Nil	Subconj.	Same group of 6, 20 da. later	2	As above	As above, then killed, 7 da. after 2nd injection
6 (repeated at 7-da. intervals 8 times)	Dead mf. in conj. biopsy on 2 occasions	Subconj.	2	2 (each time)	As above, only after 4th inj. less reaction; lid edema marked; last inj. did not cause reaction	Chronic bulbar hyperaemia and chemosis of lids after 2 months, when killed
12–20 (varied in each animal)	Fragments in sections	Iris	5	1–2	Aqueous flare & fiery hyperemia of globe. Cotton wool exudates covering pupil; in 4 out of 5 part tumbled into Ant. ch. Iris blood vessels engorged; slight chemosis of lids. All above at height in 7 da.; healing took another 3–4 wk., when 4 killed. One rabbit killed at height of reaction	Resolution began after 9 da. Exudates organized, pupil membranes shrank & split. At 21st day pupil cleared in 3 but with residual exudate at margin (rolled border) or depigmented fringe; in 2 ant. syn. & in 1 post. syn.; 1 eye had persistent occluding membrane. Where pupil clear ant. lens capsule showed color pattern, lent. opacities & free pigment granules. All eyes (4) now quiet. Control eyes very slight exudate lasted 3–4 da. & then became absorbed
2–3 (repeated in 2 rabbits after 5 da.)	Fragments in sections	Corneal stroma	4	immediate	White opacity & neovascularization from limbus. Bulbar hyperemia. One killed on 3rd da.	Part resolution in other rabbits after 2–3 wk., leaving corneal macula. Control corneae opaque for 2–3 da. only, & left no residuum. Killed about 21st da.

TABLE 1 (*Continued*)

No. Microfilariae Injected	Subsequent History of Microfilariae	Structure Involved	No. of Animals	Onset (in hr.)	Effects	Sequelae
50	Fragments in sections	Retrobulbar	2	Nil	No clinical change after 1 wk. when rabbit killed	See "Microscopic appearances" in this Part of the thesis
250 (Approx.) weekly for two mo.	Nil	Subcutaneous	4	Nil	Attempt here to produce chorioretinal changes was unsuccessful	No conclusions reached. Inserted for record

THE EFFECT OF THE FOUR ANTIGENS ON THE EYE

The experiments just described were carried out using a simple suspension of living or dead microfilariae mixed with streptomycin. The experiments with dead microfilariae were now repeated using the four antigens. Where the bodies of the parasites had been subjected to bombardment, the results were similar to those described above. In the case of the second antigen the reaction was slight; in the third and fourth the results were inconclusive by comparison with the control eyes. Heat, acetone and trichloracetic acid seem to destroy the toxin produced as a result of the disintegration of the microfilariae bodies, a toxin which leads to inflammation when not so treated.

parasites is then decanted and centrifuged at 5,000 revolutions per minute for about 10 minutes. The supernatant contains most of the microfilariae still; up to 4,000 have been estimated in 25 cc.; they can be kept alive for as long as 48 hr. provided the temperature is not higher than body temperature. Before use 25,000 units of streptomycin are added to the microfilarial suspension and 25,000 units to the control solution, which consists of Ringer-Locke solution by itself. Streptomycin does not kill the parasites, nor does it affect the ocular tissues in the amounts injected, while keeping secondary infection under full control.

Counting chambers are now filled with the suspension and the number of parasites in each chamber up to a volume of 1.0 cc. are estimated. We made up counting chambers ourselves with perspex rings. Fluid is taken with a syringe from the middle of the suspension after inverting the bottle. If the parasites are required dead the suspension is placed in ice for 48 hr. Although it has been reported that the microfilariae within onchocercomata flown to a laboratory in ice were alive several days later, ex nodule microfilariae collected in the manner described above do not survive even 24 hr. in a refrigerator. We gave them 48 hr. only for good measure.

2. PREPARATION OF ANTIGENS

Four antigens were prepared from the microfilarial suspension:

a. The suspension was subjected to supersonic bombardment at a one megacycle frequency, six watt power output, with a four cm. diameter cell for a period of 15 minutes.

b. The suspension was heated at 90°C. for one hour.

c. Two volumes of acetone were added to one volume of suspension and left for 30 minutes at 4°C. after which the acetone was evaporated off in a vacuum.

d. Trichloracetic acid two-percent was added to the suspension in equal volume, left for 30 minutes at 4°C, and then neutralized with sodium hydroxide at pH 7.0.

Streptomycin was added in the same proportion to each of the four antigens, which were then kept in ice until required.

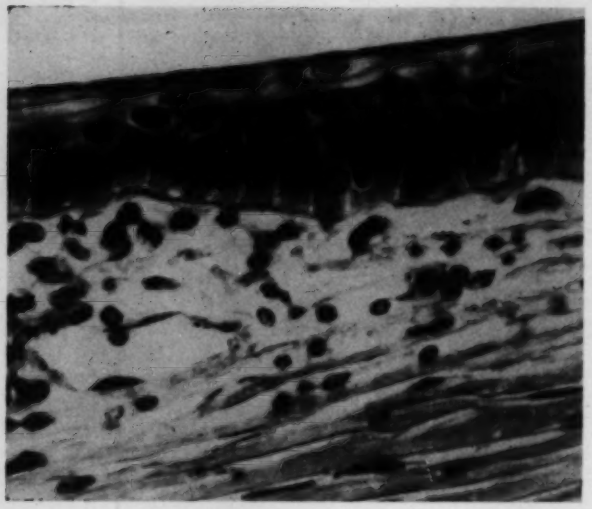


Fig. 1* (Rodger). Rabbit 12. Subconjunctival injection of *living* microfilariae repeated after a fortnight and killed two days after second injection. Corneal involvement is restricted to the most superficial lamellae of the stroma immediately adjacent to the limbus. The complete absence of eosinophil leukocytes is a notable feature. Subconjunctival edema and cellular infiltration were slight. (×410.)

3. Plan of experiments

Experiment 1. The effect of ocular injections of living and dead microfilariae and of the four antigens in rabbit eye.

Experiment 2. The active and passive transfer of hypothetical antibodies to guinea pig and rabbit eye.

Experiment 3. The effect of subconjunctival injections of dead microfilariae in blind human subjects not suffering from onchocerciasis, or suffering from onchocerciasis without ocular invasion, or suffering from onchocerciasis with ocular invasion *but without an ocular lesion.*

No experiment was carried out on onchocerciasis subjects with ocular invasion and ocular lesions, as this was considered too hazardous.

Experiment 1

The results of this experiment are summarized in Table 1.

Experiment 2

a. Active transfer of hypothetical antibodies

Each of the antigens in turn was tested on a pair of animals in a guinea pig and rabbit series, that is 16 animals in all were used. Subcutaneous injections of the antigen being tested were given from 15 to 25 days before the exciting dose was administered. The latter was given subconjunctivally in the guinea pig eye and subconjunctivally and into the iris in the rabbit eye. A state of hypersensitivity could not be elicited. In addition, the qualitative response to an equal number of dead microfilariae in the sensitized animal was identical to that in the nonsensitized. The recovery periods were also roughly the same. When the sensitizing and exciting doses were both administered locally into the ocular tissues the same negative results were obtained. There can be no question that neither with the repeated "sensitizing" injections, as described in Experiment 1, nor with the single "sensitizing" subcutaneous or intraocular injections described here, did an "exciting" dose in the eye produce an allergic reaction. There was, in other words, no suggestion at any time that a hypersensitive state existed.

---

* I am grateful to Prof. Norman Ashton of the Institute of Ophthalmology, London, for preparing these sections.

Fig. 2 (Rodger). Rabbit 11. Treated exactly as was Rabbit 12 but *dead* microfilariae were used. The subconjunctival stroma shows a diffuse cellular infiltration which consists predominantly of eosinophil leukocytes, which have formed in one area a well-demarcated and localized aggregation immediately under the epithelium adjacent to the limbus. Fragments of microfilariae are present among the cells. This is the acute phase of an onchocercal limbitis. (×260.)

b. Passive transfer of hypothetical antibodies

The purpose of this experiment, as the last, was to demonstrate the presence of an antigen-antibody system in human onchocerciasis. On the assumption that heavily infested patients had a high antibody content in the blood, it was hoped to inject into the eye 0.05 ml. of serum from such patients mixed with equal volumes of the four antigens. Subconjunctival injections of the serum alone, however, resulted in a violent inflammatory reaction in the rabbit. It was obvious that this procedure could not be used, human serum itself acting as a foreign protein. Rabbits which were sensitized to human serum died of anaphylactic shock. Guinea fowl egg albumen produced an exudative iritis similar to that

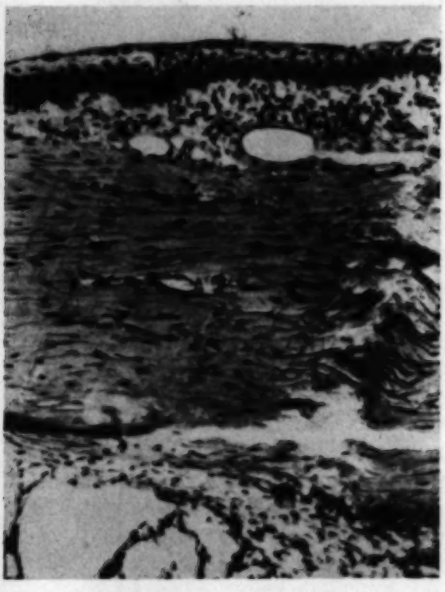


Fig. 3 (Rodger). Rabbit 23. Eight weekly subconjunctival injections of dead microfilariae and then killed day after last injection. An inflammatory pannus passes for one to two mm. into the cornea from the limbus on one side of the section lying close under the epithelium. The limbal region is vascularized and contains among the vessels eosinophil leukocytes with plasma cells. This is an onchocercal limbitis with a commencing sclerosing keratitis (×125.)

following injection of human serum into the iris. In an earlier paper[1] passive transfer of human antibodies using this technique could not be demonstrated in guinea pig or rabbit skin.

Experiment 3

a. Effect of dead microfilariae on the eye of man not suffering from onchocerciasis

For this experiment fresh suspensions of dead microfilariae were used. About 45 dead parasites were injected under the conjunctiva at the 6 o'clock position in the case of two volunteers, one blinded by cataract, the other by optic atrophy (positive Ide test). Neither suffered from onchocerciasis or the blood-borne filarial diseases. Within two hours a very violent bulbar hyperemia had developed, and the palpebral conjunctiva was like red velvet. This reaction reached its peak at the end of 24 hr., and then began to resolve. A crescent of white corneal opacification developed at the site of the injection. It took six days for the inflammation to subside. Prepared as we were for what was likely to happen, by having previously completed our animal experiments and graded the dose carefully, nevertheless, the dramatic onset of this violent reaction in the first patient was rather frightening. No harm was done, however, and the patients were subsequently handed over to hospital for treatment of their original diseases and benefited in the long run. This was done in the case of all the human volunteers.

b. Effect of dead microfilariae on the eye of man suffering from onchocerciasis but without ocular invasion

Only one subject, blinded by glaucoma, was selected. Following the subconjunctival injection of about 45 dead microfilariae from the same suspension, a less violent reaction of the bulbar conjunctiva occurred compared with the two previous cases. The hyperemia took two days to develop and disappeared in a week.

c. Effect of dead microfilariae on the eye of man suffering from onchocerciasis and with ocular invasion but without an ocular lesion

There were three subjects, all blinded by senile cataract. The same procedure was carried out as before, using the same microfilarial suspension. There was absolutely no reaction in any of the cases. This was repeated in one case immediately, but the eye still remained white. The dead microfilariae which led to such a dramatic inflammatory reaction in the other subjects had no effect on this type of case.

d. Effect of dead microfilariae on the skin of man

This was carried out on two subjects: one with an I.D.F. of 31 and the other who did not suffer from onchocerciasis or any other filarial infestation. In both, about 50 dead microfilariae were injected subcutaneously into the thigh, and the control solution placed in the opposite leg. There was a moderate inflammatory reaction in each patient, slightly more severe than that in the control limbs, and approximately the same in both subjects. These results, to be included in another paper, are inserted here for two reasons: first, the immunity or partial immunity of the eye which Experiment 3 appears to demonstrate does not apparently occur in the skin; it is in short probably a local tissue immunity. Second, the reaction of the skin need not necessarily be an allergic one; it too may be the result of a primary toxic effect, as is illustrated in the case of the second of these two subjects.

Microscopic appearances of the experimental eyes

The experiments just described gave rise to lesions clinically identical with most of the ocular manifestations of onchocerciasis seen in man; the limbitis, sclerosing keratitis, keratouveitis and anterior uveitis were clearly demonstrated. We were unable to

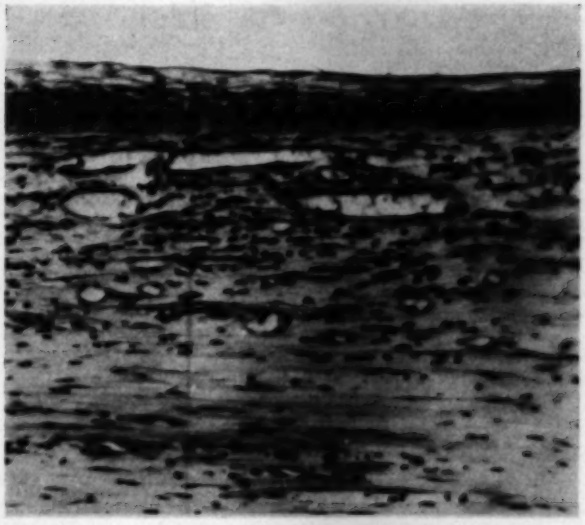


Fig. 4 (Rodger). Rabbit 8. Intracorneal injections of dead mf. repeated five days later. The animal was killed 10 days after the second injection. An inflammatory reaction can be seen involving half the stroma and consisting of an organizing subacute keratitis in which eosinophil leukocytes, lymphocytes and plasma cells are present. New vessels have grown out from the periphery quickly to the area of the injection which lay about five mm. from the limbus. This is a sclerosing keratitis associated with interstitial areas of inflammation. (×125.)

reproduce the punctate keratitis, for where only one or two dead microfilariae were placed in the cornea the resultant opacity was much bigger than those appearing in a punctate keratitis. We did not attempt to place dead microfilariae in the choroid, retina or optic nerve, although we did produce by retrobulbar injection what proved on autopsy to be a perineuritis; but there was nothing in the clinical picture to associate this with what we observed in man.

The eyeballs were embedded in celloidin and stained with hematoxylin and eosin. The microscopic appearances in the first

Fig. 5 (Rodger). Rabbit 14. Dead microfilariae placed in the anterior chamber and iris, and animal killed two days after injection. The episcleral tissues and peripheral corneal stroma show an inflammatory infiltration with numerous eosinophil leukocytes in it. It is suggested in the text that this reaction is due to fluid from the suspension of dead microfilariae having been released during the passage of the needle. The picture is one of a commencing sclerosing keratitis in a keratouveitis, exactly comparable to what is seen in man. Note cells in angle. (×75.)

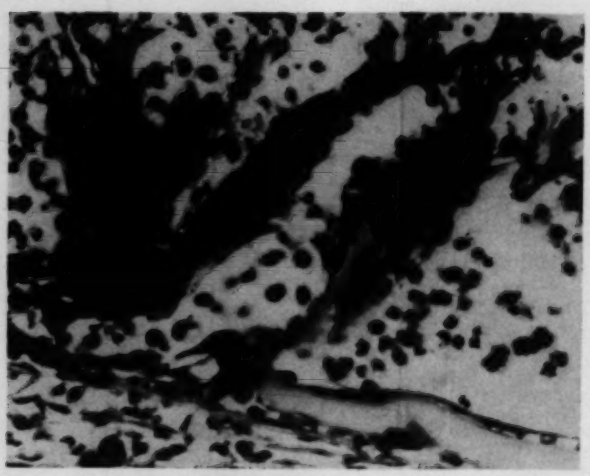


Fig. 6 (Rodger). Rabbit 14, as in Figure 5. High-power view of angle of eye. The filtration angle is encircled with eosinophil leukocytes, some monocytes and a few plasma cells. There is abundant fibrinous exudate in the anterior chamber. Blockage of the angle of the eye is a common complication of a kerato-uveitis or anterior uveitis. (×260.)

paragraphs below are given under the clinical heads of the ocular lesions so they may be compared the more readily with the descriptions of the human pathology reported in Part IV. There is one important difference in the two groups, which must be underlined at the start. The animal eyes for the greater part (but not entirely) represent the acute stages of the disease in the different structures of the eye, while the human represent the subacute or the chronic.

1. PRIMARY EXOGENOUS INFLAMMATION AROUND DEAD PARASITES

a. *Limbitis.* The tissue in the region of the limbus where subconjunctival injections of dead microfilariae had been made, was markedly edematous and showed a diffuse infiltration in which eosinophil leukocytes and lymphocytes were present. The infiltration extended into the superficial half of the corneal stroma for a few mm. and also in a posterior direction into the episcleral tissue

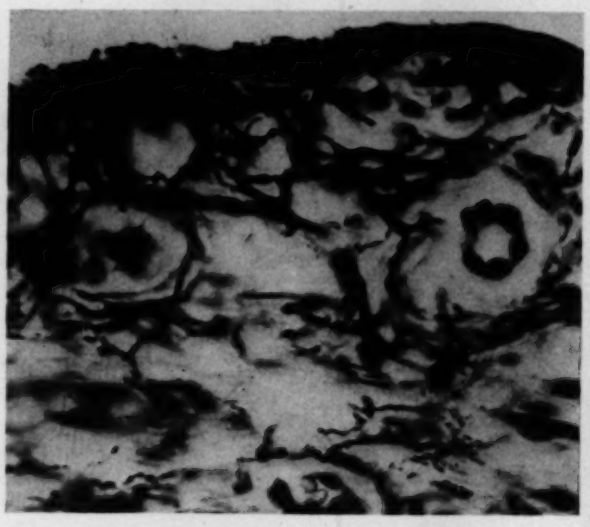


Fig. 7 (Rodger). Rabbit 14, as above in Figures 5 and 6. High-power view of iris. Over the surface of the iris there has formed a fine organizing membrane. There is a diffuse eosinophilia in the iris vessels, the endothelium of which is swollen, and in places occludes the lumen. The stroma exhibits a fibrinous exudate in which many eosinophils are present. The pigment cells have moved forward to the anterior face forming a solid barrier underneath the surface exudate. This is an onchocercal anterior uveitis. (×520.)

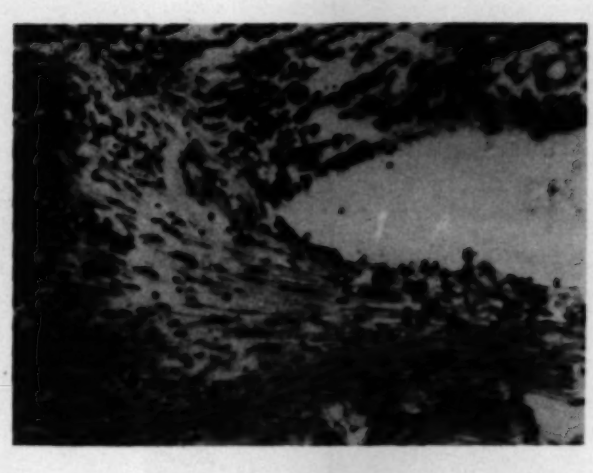


Fig. 8 (Rodger). Rabbit 3. Dead microfilariae injected into the iris directly (a heavy load) and the animal killed six weeks later, when the condition was subacute to chronic. The filtration angle is blocked with organized exudate in which many plasma cells and a few monocytes and eosinophils are present. In the root of the iris a few hyaline spherules can be seen. This is the classic picture of onchocercal anterior uveitis in man. (×125.)

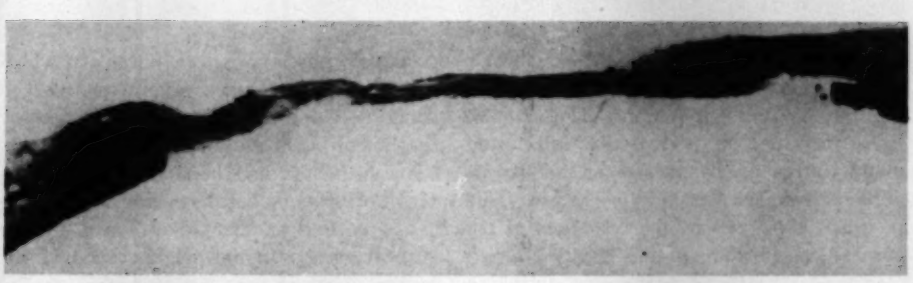


Fig. 9 (Rodger). Rabbit 3, as in Figure 8. An organized membrane occludes the pupil, as in man (×28.)

Fig. 10 (Rodger). Rabbit 21. Same treatment as for Rabbit 3. Fibrous tissue has proliferated within the iris stroma. The vascular endothelium is swollen and some vessels occluded. There is a chronic inflammatory cell infiltration throughout; the posterior pigment epithelium forms a solid band on the posterior face but the band of chromatophores along the anterior face is breaking down and thinning out, signifying healing. This is characteristic of the iris in a chronic anterior uveitis due to onchocerciasis. (×125.)

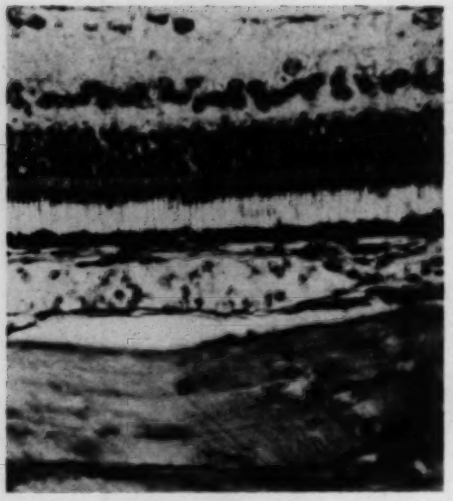


Fig. 11 (Rodger) Rabbit 33. Subcutaneous injections of dead microfilariae were given weekly for two months in an attempt to poison the retina or the choroid. No abnormality of the posterior segment of the eye exists. This specimen is stained with Masson, unlike the others all of which are stained with hematoxylin-eosin. (×460.)

and even into the sheaths of the extraocular muscles. The advancing edge of the corneal infiltration consisted mainly of eosinophil leukocytes, and the perivascular infiltration of the conjunctival vessels at the limbus was derived from the lymphocyte element. This no doubt explains why the resolution of the corneal opacification in the lightly affected case was complete. The iris was quiet and unaffected. Invasion of the cornea by small capillaries, accompanied by the usual cells, more particularly in repeated infections, occurred, the new vessels passing under the epithelium and above Bowman's zone. There is, of course, no Bowman's membrane in the rabbit.

b. *Sclerosing keratitis.* The cornea in the neighborhood of the dead microfilariae placed in the stroma revealed peripheral vascularization and an organizing subacute keratitis. The dominant cells were eosinophil leukocytes and lymphocytes among which a few plasma cells were present. The eosinophils were present in large numbers at the advancing edge of the pannus beyond the foremost vessel. The latter lay close under the epithelium; fibroblasts were also seen passing along with the vessels from the limbal area; it was not possible to say whether they were corneal corpuscles or scleral fibroblasts which had invaded the cornea. There was marked congestion and perivascular infiltration of the limbal blood vessels outside the cornea, some of which had become occluded as a result of the endothelial swelling.

c. *Anterior uveitis.* Involvement of the corneal margin in the neighborhood of the needle puncture was not altogether due to trauma by comparison with the control eye. It may be that the fluid of the microfilarial suspension contained some toxic products of the microfilariae within it, and that that caused the keratitis which developed around the track of the needle. The main effect, however, as was intended, was seen in the anterior uvea, in the iris and ciliary body, especially the former into which microfilariae had been injected.

The affected part of the cornea reflected to a minor degree the picture seen in sclerosing keratitis, and may be quickly dismissed. The vessels of the limbal circle were very congested and cuffed with inflammatory cells. There was also constant involvement of the ciliary body, although in none of these eyes had microfilariae been placed in that structure. This was more than vascular congestion; plasma cells and an occasional nod-

Drawing 1* (Rodger). The development of a sclerosing keratitis from a limbitis in the rabbit eye.

Drawing 2 (Rodger). Resolution of the fibrinous exudate covering the pupil in the rabbit eye, until it is fully organized and reveals splits in the membrane.

Drawing 3 (Rodger). The same as Drawing 2, only this time there was a greater amount of exudate, some spilling over into the anterior chamber. As a result after partial resolution the pupil was deformed adopting the pyriform appearance characteristic of the lesion in man.

ule of lymphocytes in the ciliary body were seen in some eyes. One assumes that toxins had diffused there from the iris.

The iris itself was severely affected. The chromatophores of the stroma migrated in large numbers to the anterior face and there formed a solid band. The posterior epithelium became swollen and darker. There was an infiltration of eosinophil leukocytes with some lymphocytes, plasma cells, and an occasional monocyte also present. The endothelium of the vessels had swollen and in places they were occluded. The space normally present in the iris arteries could not readily be distinguished.

Finally, an inflammatory exudate was present not only within the iris but also in the anterior, and sometimes the posterior, chamber; occasionally exudate lay on the surface of the anterior part of the retina. A cyclitic membrane was well formed in some. The filtration angle of each of the eyes, although to varying degrees, was encircled with organizing fibrinous exudate in which many inflammatory cells could be made out. Where the occluding membrane over the pupil persisted it was fully organized; posterior synechias or ectropion of the pigment fringe were also noted. In two eyes the lenses showed early cortical opacities.

d. *Optic perineuritis.* The nerve itself was not affected, and appeared healthy. There was suspected congestion of the septal vessels. Inflammatory cells were present in

* These drawings were done by me directly from experimental eyes.

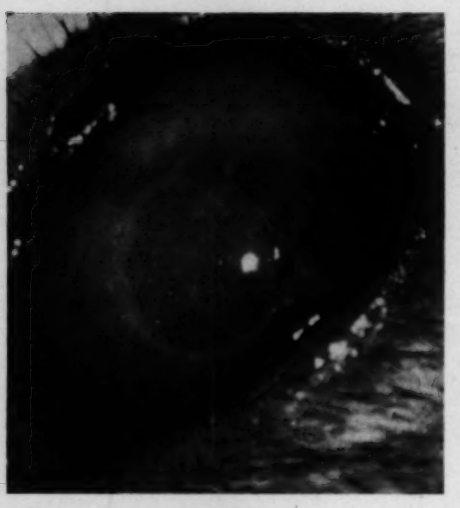


Plate 1 (Rodger). Early appearance of exudate in rabbit eye at pupillary border after injection of dead microfilariae into the iris.

abundance in the subarachnoid space, consisting for the greater part of lymphocytes. Eosinophil leukocytes were present in large numbers in the adjacent posterior ciliary vessels.

2. Possibility of inflammation being induced by exotoxins from living microfilariae

Where living microfilariae were placed under the conjunctiva, edema and infiltration were slight and variable in degree and corneal involvement negligible. *The total absence of eosinophil leukocytes was a feature.* In those animals where living microfilariae were placed in the anterior chamber and iris, no inflammatory changes at all were observed in the sections other than a little albuminous exudate, probably post mortem in origin. As the changes, minor though they were, were significantly greater than those seen in the control eyes there must be some explanation for them. Either living microfilariae do secrete an exotoxin, or one or two died, perhaps, before the suspension was injected, or maybe their movements when up against a barrier, like the inner pupillary ring, led to irritation.

As not every eye gave evidence of these changes (slight aqueous flare, hyperemia and exudation at the pupil), and as they disappeared within a few days of onset, we are inclined to believed that the last of the three explanations is the most probable.

3. Onset of tolerance with repeated infections

The subconjunctival tissues into which dead microfilariae were repeatedly injected, when finally examined, showed marked edema and a diffuse chronic-inflammatory-cell infiltration, in which plasma cells dominated; eosinophil leukocytes and lymphocytes were present but in decreased quantity. This series of animals was the first where the condition might be classified as chronic; as it turned out the microscopic appearances exactly corresponded with those we found later in man.

The sector of cornea adjacent to the area of limbitis was vascularized and some chronic

Plate 2 (Rodger). Healed quiescent anterior uveitis after two injections of dead microfilariae into the rabbit iris. An inflammatory membrane persists. (Same eye as section in Figure 9.)

inflammatory cells and fibroblasts had invaded the superficial stroma. Some patches of interstitial keratitis were present, although microfilariae had not been placed in these areas and no sign of microfilarial fragments were visible. One assumes these patches arose from the diffusion of toxins from the primary focus.

The anterior chamber contained a small amount of exudate, but that was all; the exudate was albuminous and there were no cells.

Considering the great reaction and severe structural changes which result from a first injection of parasite bodies, the microscopic changes after repeated injections confirm the clinical evidence that the ocular tissues become locally immune, or partially so at least.

The appearance of pannus in the interstitial layers of the cornea, where no microfilariae had been placed, was a new and interesting feature, and probably reflects what happens in the human eye. Several microfilariae in the process of dissolution were found in the subconjunctival tissue at the site of the last injection. The two rabbits were killed three or four days after the last injection, at which time there was no change in the clinical appearance existing before that injection, namely a chronic mild irritation. The pathology supports this observation.

4. Possibility of allergy after sensitization

With the first three or four injections into the eye we observed the same degree of inflammation. Being able to grade the dosage it was possible to assess the probable degree of the reactions, and to forecast them. Sensitization by repeatedly injecting the parasites into the eye, as we have shown above, did not produce allergy (hypersensitivity). Hyposensitivity resulted instead. Sensitization by administering the dead microfilariae as an antigen and then about 15 days later giving a shocking dose provided no evidence that a hypersensitive state could be created in this way any more than by repeated injections. The clinical and microscopic appearances were similar no matter whether it was the first, second, third or fourth injection divided in point of time by one, two or three weeks. The so-called shocking dose, given after the period of time usually prescribed for antibody formation, did not produce a reaction any more violent than did a second injection given within this period.

5. Changes in the control eyes

The effect of the Ringer-Locke-streptomycin solution on the eye was slight and inconstant and usually disappeared in a couple of days. It consisted of a slight granular exudate in the anterior chamber, sometimes in the posterior also, and around the perforating wound, site of the original injection, a slight inflammatory infiltrate. Eosinophil leukocytes were noticeably absent, and the infiltrate was strictly localized. Where the needle had penetrated the iris there might be a few inflammatory cells, or nothing at all. Slight vascular congestion at the limbus at the site of the limbal puncture was general, but quickly settled. The eyes excised several days after the initial operation (five to 60 approximately) revealed no abnormality. As a result of these findings we have every confidence that the structural changes in eyes treated with microfilarial suspensions depended entirely on the presence of the parasite bodies.

Discussion

There is no doubt that the clinical lesions produced in the animals in the experiments just described exactly represent those seen in man. We reproduced the limbitis, sclerosing keratitis, interstitial keratitis, and anterior uveitis in full detail. The acute phase is brief, and it seems that within a matter of one or at the most two weeks the picture of an established chronic ocular lesion presents itself. Thus the animal experiments afforded evidence of the most important kind of what we alone had previously concluded on clinical grounds, namely that an acute phase does

occur in man, contrary to past opinion (Rodger[8]).

To be able to observe the acute attack from its onset to its resolution by slitlamp and to note how complications arise, all fitting into the clinical pattern seen in man where they are revealed at different stages like a jigsaw puzzle, was most enlightening.

With the knowledge that ocular onchocerciasis does lead to occlusion of the pupil, does cause exudate to drag the pupillary margin down, that the exudate does tend to resolve in whole or in part, and frequently leaves a "rolled border" of organized tissue at the pupil, or if it completely resolves, uncovers a depigmented pigment fringe with or without synechias, with or without lenticular opacities, and so on, greatly strengthens one's confidence in making a diagnosis. It is an experience to be recommended. For this reason alone, therefore, the experiments were worth while, although that was not their main purpose. We wanted to try and formulate the pathogenesis.

There seems little doubt that the essential factor is death of the microfilariae in the tissues concerned. The reaction is immediate and violent in an eye not previously infected. With repeated infections, it was clearly demonstrated the tissues become less and less sensitive. This state of tolerance appears to be a property best defined as a local immunity, and does not appear to occur in the skin of man. The opposite state of affairs, hypersensitivity of the eye to repeated or sensitizing injections, we failed to demonstrate. Perhaps this claim should not be unduly pressed, because these latter experiments were not altogether comprehensive. More work must be done in the case of the human eye.

One thing that did emerge clearly was that it is the dead and not the living parasites which have a primary toxicity. It is not easy to explain the mild inflammatory reaction which occurred in some of the eyes into which living microfilariae had been injected. It may be, as I have suggested earlier, that the original suspension had been slightly contaminated with microfilarial toxin by one of them having died before the injection was administered, but that would not explain the delayed reaction which occurred in some of the animals. This reaction admittedly was slight and transient, but it none the less requires an explanation. We do not accept it as evidence that the living microfilariae secrete an exotoxin. It is more probably due to mechanical irritation, such as might happen if a parasite became entangled in the stroma of the iris, or kept pushing away at the pupillary margin. One only needs to observe the activity of the parasites under the microscope in iris or corneal biopsies to accept this theory more readily.

The fact that we did not always observe the microfilariae we had placed in the anterior chamber was at times disconcerting, but is fully in accord with our experiences in man, where eyes revealing no signs of parasites in the aqueous humor when subsequently examined microscopically revealed their presence. They appear to be photophobic, and hide behind the iris. The fact remains that they were observed at times. So, the evidence is quite strong that living microfilariae do not secrete an exotoxin. The technique holds out fascinating prospects for future work.

Probably the most important of all the experiments were those on man. The total absence of any reaction whatever when dead microfilariae were placed under the conjunctiva of patients suffering from onchocerciasis with positive conjunctival biopsies *but without ocular lesions* could not have been more striking, especially as I had previously demonstrated with similar dosages a particularly violent reaction in patients who were not suffering from onchocerciasis. There is no question here that the dead microfilariae have a primary toxicity in man, and that in some infected subjects an immunity exists.

It is a pity I did not carry out any experi-

ment in patients exhibiting some of the manifestations of *ocular* onchocerciasis, but the reader no doubt understands my reluctance to do so. It is impossible to be sure that a state of tolerance has arisen; it need not necessarily have been reached even in a blind onchocercal eye, so I argued; to produce an endophthalmitis leading to great pain and total destruction of the eye was a prospect unpleasant to contemplate and ethically indefensible; eyes with previous lesions might even be hypersensitive; we have no human evidence precluding this, although it seems unlikely.

The local ocular immunity demonstrated in man could not be explained by any of the animal experiments; in the latter we only demonstrated the development of such an immunity with repeated infections, each in itself potentially a destructive one. One assumes that it all depends upon the weight of the initial infections. The death of a single microfilaria in the eye might lead to little or no visible evidence of an inflammatory reaction ever having occurred, yet might lead to partial immunity; on the other hand, if, as in our experiments, a number of parasites happened to die in the eye simultaneously on the first occasion, then an ocular crisis would almost certainly result. This is given indirect support by the fact that I frequently noted in the course of routine examinations with the slitlamp the relation of living microfilariae in conjunctival biopsies, or in the anterior chamber, with only very minor signs of disease; a common one was the presence of pigment granules on the anterior lens capsule in young persons, or of a small quiescent tongue of pannus onchocercosus.

These are interesting conjectures, which cannot be proved until the toxic product of the dead microfilariae, evidently destroyed by heat, acetone, and trichloracetic acid, is identified, isolated and tested further. That tolerance of the type we demonstrated in rabbits occurs in man, we have no doubts; we believe it to be widespread and common. Where intraocular microfilariae in a subject with an ocular lesion are killed by diethylcarbamazine, there is not always a recrudescence of symptoms. The literature is full of such apparent contradictions; here is the explanation—these patients have acquired a partial immunity.

The microscopic appearances of the experimental eyes supply a few other facts worth emphasizing. One is that the acute phase is characterized by the presence of eosinophil leukocytes. Their exact relationship to the dead microfilariae was better understood in the human material we studied, and will be given later in Part IV. Another point of importance is that the dissolution of the parasites is not associated with the presence of macrophages or giant cells, which is surprising, and warned us to look for other evidence of microfilarial dissolution when we came to examine the human eyes.

Another point is that the nature of the infiltrate changes rapidly from one in which eosinophil leukocytes dominate to one where plasma cells are present in great numbers. This confirms the belief that the acute phase is short. The development of pannus, hugging the undersurface of the epithelium, comparable to its characteristic position in the human eye, is rather difficult to understand. Why this preference for Bowman's zone? We had always supposed that the situation of pannus onchocercosus in man's eye between Bowman's membrane and the epithelium depended on the fact that the microfilariae preferentially passed in that direction as being the locus minimae resistentiae, and on dying there led to pannus formation. But here we placed dead microfilariae in the eye of the rabbit either subconjunctivally or into the corneal stroma, not necessarily just underneath the epithelium—the technique could not be as accurate as that; yet the new capillaries always passed between Bowman's zone and the epithelium. There may be some simple explanation of this phenomenon which has escaped my attention.

Another interesting feature which emerged from these studies of the histopathology was the presence of interstitial keratitis in areas deep to the site of the injection. As the site could be localized accurately by the corneal wound there can be no doubt of this. The assumption that toxins emanating from the dead parasites diffuse through the cornea and lead to these localized patches of inflammation seems a reasonable one. The same argument explains the onset of a sclerosing keratitis following repeated attacks of experimental limbitis.

In all respects the microscopic appearances of the experimental eyes dovetail well with those found in the human, provided it is not forgotten that on the whole the animal eyes were excised during or at the end of the acute phase and the human at the beginning of or during the chronic phase. Where I did obtain an acute eye in the human the pictures corresponded, the opposite also being true.

Conclusions

1. The inflammatory reaction in ocular onchocerciasis is a primary intoxication depending on the presence of dead microfilariae. The unsensitized eye is highly susceptible.

2. Living microfilariae may cause slight irritation with a correspondingly slight and transient inflammation, probably when the local cytoarchitecture hampers them in their movements.

3. It is almost certain that the toxins diffuse from the primary focus to neighboring tissues. Involvement of the interstitial corneal stroma and the ciliary body can only be explained in this way in the experimental eyes.

4. Some human eyes were found to be immune to the microfilarial toxin or toxins. Other eyes appeared to have a partial tolerance. It is suggested that local immunity can arise in the eye if the number of microfilariae which dies in the eye on the first few occasions is low. In eyes apparently immune there can usually be found evidence of a slight inflammatory reaction having occurred in the past, which lends support to this hypothesis. In support of the claim that an acquired partial tolerance occurs, the usual clinical history of the disease—a few acute attacks becoming less frequent and less acute until inflammation is mild and chronic, even in eyes still heavily invaded—fully supports this view.

5. Hypersensitivity to the microfilariae does not appear to occur. We were unable to demonstrate in experimental animals the presence of antibodies by active transfer. Intraocular passive transfer was impossible because human serum acts as a foreign protein.

6. It is generally believed that the skin becomes hypersensitive to microfilariae volvulus. There is no evidence, however, other than equivocal, to show that the reaction in this structure, supposedly sensitized, is any greater than it is in a primary infection. Signs attributed to allergy when a microfilaricide is given in dermal onchocerciasis might equally well occur as the result of a heavy primary intoxication, especially when so many parasites are being simultaneously killed. Among the signs to which we refer are headache, arthralgia, raised temperature, reaction to antihistamines and even edema. The transient eosinophilia which results cannot be used as evidence of allergy as we are dealing with a filarial infestation anyway.

References

1. Rodger, F. C.: Bull. World Health Organization, **16**:495, 1957.
2. Rodhain, J., and Dubois, A.: Tr. Roy. Soc. Trop. Med. & Hyg., **25**:377, 1932.
3. Toulant, P.: WHO unpublished report, 1953.
4. Rodhain, J.: Ann. Soc. Belge Med. Trop., **29**:177, 1949.
5. Sulzberger, M. B.: J. Allergy, **21**:85, 1950.
6. Rodger, F. C.: Brit. J. Ophth., **41**:599, 1957.
7. Strong, R. P.: Onchocerciasis. Cambridge, Mass., Harvard Univ. Press, Part VIII, 1934, p. 78.
8. Rodger, F. C.: Brit. J. Ophth, **41**:544, 1957

Part III: The posterior segmental lesion*

General indications

The posterior lesion is the most interesting manifestation of onchocerciasis because it is the least understood. Bryant,[1] after a conversation with the Belgian worker, Hissette, reached the conclusion that a progressive chorioretinitis which he has seen in the Sudan was caused by onchocerciasis. This opinion, later supported by Hissette[2,3] and by Richet,[4] has since been confirmed by the observations of many other workers. The current view when this study was started was that the cause of the condition is invasion of the choroid by the parasites and their death. Bryant[1] could find no evidence of this. The belief was given some support by the finding of microfilariae in the choroid by Ochoterena[5] and Hissette[2]; one autopsy case with several microfilariae in or adjacent to this tissue was also reported by Hughes.[6]

When we started our investigations into onchocerciasis in West Africa we visited first a very heavily endemic area in the Northern Territories of Ghana. There many examples of the posterior segmental lesion were found, and nearly all of them (as it was a heavily endemic area) in densely infested subjects. Subsequently, however, we surveyed Northern Nigeria, and here, in areas of light endemicity, the incidence was paradoxically higher. The lesion was a localized posterior choroidal sclerosis.

Having evolved by this time an index of the density of infection in the individual (Rodger and Brown[7]), the index figures were compared in cases of anterior and posterior lesions in Nigeria. The results were extremely interesting. Whereas, the mean individual density figure for the anterior lesion was about 26, it was 11 for the type of posterior lesion under discussion; four cases had sterile skins and conjunctiva, and of these two had no nodules although the lesions were characteristic.

This raised a problem of pathogenesis, for it no longer appeared so certain that the cause of the condition was an inflammation arising around the dead bodies of microfilariae in the tissues concerned. In the heavily endemic areas of Ghana we seldom saw the posterior lesion except in association with an anterior lesion, but in Nigeria this was far from being true; nine percent of 165 recorded cases were associated with a sclerosing keratitis, two percent with a keratouveitis, and nine percent with an anterior uveitis; 80 percent, in short, were not associated with anterior lesions.

Another factor which suggested that there might be more to the pathogenesis than the accepted view concerned the average number of nodule sites in the different types of lesion. Where the posterior lesion occurred alone, the average number (nodule mean) was 0.9; when the posterior lesion was combined with the anterior segmental lesion in the same geographic areas the average was 2.0; with anterior segmental lesions alone, it was as great as 2.6. The possibility that another factor might be involved thus gained strength.

This view was lent further support when it was observed that in high-forest areas (where onchocerciasis is common although not severe) no posterior lesions were discovered, whereas in the Northern scrub, *even in areas with equal density quotients*, the posterior lesion was extremely common. For these reasons, therefore, it was concluded that although onchocerciasis plays some part in producing this lesion, as it has not been reported from places outside the endemic onchocerciasis areas, another factor or factors must be sought.

Discussion of clinical features

The different diseases which bear some resemblance to the posterior segmental lesions

* This is the only part of the thesis which has previously been published (Rodger, F. C.: Brit. J. Ophthl., **42**:21, 1958.) It is included so that all aspects of the pathogenesis may be considered together. It is a revised version of the original. I am grateful to the editors of the *British Journal of Ophthalmology* for permission to reprint it.

of onchocerciasis suggest that it is not an easy diagnosis. With the recognition of an exogenous chorioretinitis of onchocercal origin (Rodger[8]), as distinct from a degenerative lesion, the diagnostic features become somewhat clearer. It is hoped that when the pathology of these two lesions is presented in this thesis that this important distinction will be accepted more widely.

The imflammatory type of posterior lesion has not been seen with certainty apart from anterior involvement, although theoretically it might occur as an isolated phenomenon. In my original paper I called it a posterior *exudative* uveitis (or chorioretinitis) because that describes its exact pathology, as will be shown later. Exudation, however, occurs early and is not a marked clinical feature, so the term may be omitted. Choroidal sclerosis regularly follows the initial brief reaction around the parasites and becomes a prominent feature in a large proportion of cases. As the inflammatory changes are greatest where microfilariae die in the choroid or retina so these areas can usually be made out in the affected fundus, even where sclerosis is advanced; pigmentary aggregation for one thing is gross at these old inflammatory foci. There is never any suggestion of the lesion being posterior and circumscribed; it is most frequently observed involving a sector of the fundus, or passing back from the equator.

As for the degenerative type of posterior lesion, which I believe may prove in the end to be a separate clinical entity, the description with which I am most in agreement is that of Ridley,[9] who described the lesion in its advanced condition, with or without the corpuscular aggregation of retinal pigment at the periphery (found in a minority of cases). Ridley does not emphasize sheathing of the retinal vessels, an observation on which Sarkies,[10] Toulant and Boithias,[11] and Budden[12] lay great stress. Most authors will agree this sign is nonspecific and of little value as an aid to diagnosis. The vital feature characterizing the Ridley fundus is its location in the posterior fundus and the fact that it is circumscribed and discrete and, additionally, that there is *loss* of pigment not aggregation as in the inflammatory type. At the same time there exists in onchocerciasis cases a diffuse choroidal sclerosis where there is no circumscription; this is what I have already described as the late stage in the exogenous chorioretinitis, for never have I failed to find some suspiciously inflammatory focus in these diffusely affected fundi. Choyce[13] believes both these lesions represent tapetoretinal degenerations of the type described by Sorsby.[14] The high incidence, however, and the fact that experienced workers in this field have never in Africa observed a posterior segmental lesion of any type except in onchocerciasis patients in onchocerciasis areas suggest Choyce is wrong. Thus, by the degenerative type of posterior lesion, now to be discussed, I refer to that lesion first seen by Bryant and Hissette but first clearly described by Ridley.

Hissette and Bryant appear to have confused the inflammatory with the degenerative type. Hissette describes photophobia and lacrimation as part of the symptomatology, which is something I myself never observed. He also says that the lesion is a late symptom of onchocerciasis, whereas in my own cases it appeared to be the opposite. Hissette finds difficulty in deciding whether cupping of the disc, which is frequent, is atrophic or glaucomatous, because in many cases the cupping exactly simulates the glaucomatous type. A secondary glaucoma was common in my cases of onchocercal exudative uveitis, but glaucomatous cupping was never seen in the degenerative lesion, although atrophic cupping was usual in longstanding cases.

Toulant, Robineau, and Puyuelo[14] also appear to have been confused by the multiplicity and diversity of the lesions. I have never seen the retinal hemorrhages nor the colloid bodies which Toulant describes at the posterior pole save in the inflammatory

condition. Nor is it clear what he means when he says that he has never noted the pseudotapetoretinal degeneration of Ridley, unless there is some confusion here in the nomenclature. This term well describes what is the most characteristic stage of the disease. Toulant and Boithias qualified this statement later by saying that a secondary retinitis pigmentosa is seen but is rare, only three cases having been recorded in the course of several years' work; this is not my experience. One significant remark of theirs is that a juxtapapillary chorioretinitis is a frequent finding. This is my own view, the lesion usually first appearing in such a position. Toulant and his colleagues, who have produced much fine work on this subject, disagree with Hissette over the symptomatology, and are in general agreement with other workers that it rests entirely on the presence of hemeralopia.

All these points suggest that the variable appearance of the lesion so emphasized by Hissette, Bryant, and others is due to lack of understanding that we are dealing with two conditions. In fact, the former worker stated that he found it impossible to suggest a pathogenesis to cover the many aspects of the disease; he was not helped, of course, in that the pathologic material obtainable at the time was extremely small. Both Hissette and Bryant, nevertheless, must be given every credit for being the first to describe the changes.

Some new observations relevant to the pathogenesis

The absence of the posterior degenerative lesion of onchocerciasis observed by us in West Africa in regions where the diet contains a large amount of vitamin A is believed to be highly significant (table 1). An attempt was made to ascertain, both by assays and by clinical trials, whether vitamin A deficiency was implicated or not. In a rural community in the Plateau province of North Nigeria, where the intake of vitamin A was marginal, the sera of several cases were assayed. All the subjects came from neighboring villages except the last (Serial No. 1,291). One patient had syphilitic chorioretinitis.

Table 2 shows that the one nononchocerciasis case had a marginal level of vitamin A, whereas only one of the posterior lesion cases (Serial No. 1,291) could be placed in that category. The latter patient was examined at a different time of year, when vitamin A in plenty had reappeared in the diet, and this offers a ready explanation of the anomaly.

The situation at this point may be summarized as follows:

1. The posterior degenerative lesion is found in subjects with a low I.D.F. (mean I.D.F. 11), but is not found in nononchocerciasis areas.

2. Cases with the posterior lesion have a low nodule mean (0.9).

3. The posterior lesion is not found in areas where an abundance of vitamin A is present in the diet.

4. It was established in a group of subjects in an area where the intake of vitamin A was (on European standards) marginal, that cases exhibiting the lesion had a lower quantity of vitamin A in the plasma than might be expected.

It seemed reasonable, then, to carry out clinical trials with massive vitamin A therapy to ascertain whether or not any recovery in the visual acuity occurred. Details of the trials are given in Table 3.

The lack of success of such therapy in the control cases need not be emphasized; it was only to be expected. In four cases exhibiting the lesion, the recovery of vision could be classified as almost complete, and in three as partial. When the effect of the therapy is analysed, some interesting facts emerge.

The best results were naturally obtained in cases with early lesions, that is, those with a history of night-blindness, who showed early sclerotic changes around the disc with

TABLE 1

AVERAGE DAILY NUTRIENT INTAKE OF ADULT MALE NIGERIAN PEASANTS IN FOUR REPRESENTATIVE AREAS, 1954–1956*

Group		A	B	C	D
Occupation		Farming and fishing	Farming	Farming	Farming
Area		Banks of Lake Chad. Sahel savannah	Bunga-Ningi, Bauchi Prov. Sudan savannah	Langai, nr. Panyam. Plateau Prov. Montane	Mbanege, Ogoja. Rain forest
Lesions		No Onchocerciasis & no Ridley fundus	Onchocerciasis and Ridley fundus	Onchocerciasis and Ridley fundus	Onchocerciasis but no Ridley fundus
Calories		3,000	2,900	2,600	2,400
Protein	Animal (gm.)	29	11	15	3
	Vegetable (gm.)	78	84	81	62
Fat (gm.)		37	40	45	31
Calcium (mg.)		1,390	880	612	640
Iron (mg.)		56	37	30	23
Vitamin A (i.u.)		1,200	4,240	4,100	11,900
Thiamine (mg.)		3.6	2.9	2.3	2.1
Riboflavin (mg.)		1.1	1.4	1.3	1.0
Nicotinic Acid (mg.)		27	24	24	16
Ascorbic Acid	Uncooked (mg.)	24	133	43	316
	Cooked (mg.)	12	44	12	54

* These four areas correspond with those in which we worked. The cases quoted in Tables 2 and 3 come from Area C. The intakes were measured by methods described by Nicol[37] (1956).

or without edema or pigmentary disturbance at the macula, but partial success can be attained even when the ophthalmoscopic picture reveals a fairly gross lesion. Little or no improvement was achieved in two cases where peripheral pigmentary corpusculation existed, and the improvement was slight in those where atrophic cupping of the disc was present; these two appearances would seem to be contraindications to therapy.

It is difficult in this small series to generalize as to when or when not it is worth while attempting treatment with vitamin A, but it may be said that, where the visible choroidal blood vessels are red in color, there lies the greatest hope of recovery. Gross macular upset and optic atrophy do not appear to militate against the achievement of some improvement.

The effect of these massive doses of vitamin A was dramatic in some cases and produced quite a sensation in the village concerned. For example, one man (829) who had taken to begging, returned to his farm, and when we visited the village a year later during the rains when the farmers were busy in their fields, he was working happily among them. Another case (772), who had been completely blind, returned to market as a petty trader, where he would certainly need to use his eyes. A third (1,291), gardener to a European who was witness to his visual recovery, gained a new lease on his job.

Where possible, we controlled the degree

TABLE 2

RESULTS OF SERA TESTING

Serial No.	Vitamin A* (i.u./100 ml plasma)	Lesion
829	30	P.S.L.
830	10	P.S.L.
831	10	P.S.L.
845	20	P.S.L.
872	25	P.S.L.
879	80	Syphilitic chorio-retinitis
883	45	P.S.L.
900	20	P.S.L.
1,029	42	P.S.L.
1,291	88	P.S.L.

* A value of vitamin A below 70 i.u. per 100 ml. plasma is taken as subnormal.

of the hemeralopia with a portable dark adaptometer. The set was standardized on an arbitrary scale at a figure for normal eyes of 2.2 after 30 minutes in total darkness. In early cases the figure obtained lay between 4.0 and 5.0; in some cases the brightness of the flash threshold had to be doubled before seen; in others (even a few of the early cases) the test could not be performed at all. It was impossible to carry about a heavy apparatus like the Goldmann adaptometer so our results were comparative only. Although resolution of the anatomic changes did not occur, the dark adaptation returned to normal in early treated cases.

The Snellen charts for illiterate subjects (Landolt C and E) were used for testing visual acuity. It could be argued that the results of these tests varied according to the part of the functioning retina which was directed toward the letters. It was not possible to carry out adequate perimetry with this type of subject to ascertain which parts were healthy but every effort was made to eliminate such a source of fallacy at the initial examination. This was done by encouraging head-tilting, and the results here showed fairly conclusively that only a little if any variation in the acuity occurred at all (letters not lines).

On subsequent examinations the same practice was carried out, so that the subjects were given every chance to see the charts under equal conditions on each occasion of testing. Guessing was soon discovered. Objectively, there was no doubt when recovery of vision had been obtained. Whether such recovery was maintained, we do not know apart from the three cases quoted above. We are satisfied that no improvement occurs in the visual acuity after a course of any filaricides; only with vitamin A. Diethylcarbamazin does not alter the condition in any respect.

TABLE 3

VISUAL RESULTS AFTER VITAMIN A*

Serial No.	Visual Acuity						Lesion	Improvement in Visual Acuity
	Before Treatment		After One Week		After One Month			
	R	L	R	L	R	L		
772	H.M.	C.F.	6/36	6/36	6/36	6/12	P.S.L.	Yes
789	6/24	6/24	6/18	6/18	6/18	6/18	P.S.L.	Yes
829	6/60	6/60	6/24	6/12	6/12	6/12	P.S.L.	Yes
830	H.M.	H.M.	6/60	6/60	6/60	6/60	P.S.L.	Yes
831	C.F.	C.F.	No change				P.S.L.	No
837	6/9	6/9	No change		6/12	6/12	Syphilitic neuroretinitis	Worse
845	H.M.	H.M.	6/60	6/60	6/60	6/60	P.S.L.	Yes
924	6/36	H.M.	No change				Disciform degeneration of macula	No
930	H.M.	H.M.	No change				Disciform degeneration of macula	No
1,291	6/60	6/60	6/36	6/18	6/18	6/18	P.S.L.	Yes
1,306	6/36	H.M.	No change		Did not return		P.S.L.	No
1,338	6/36	6/36	6/9	6/6	6/6	6/6	P.S.L.	Yes

* Treatment consisted of 165,000 i.u. vitamin A daily, prescribed as five capsules Crooke's vitamin A.

Conclusions as to the pathogenesis

It is now possible to consider the probable course of events in the evolution of the degenerative lesion. It seems likely that the initial symptom of night-blindness depends upon a vitamin-A deficiency. It may be that the first appearance of retinal pigmentary disturbance in the area between the macula and the disc (juxtapapillary) is related to the high incidence of rods in that area; the rods are most dense directly below the papilla, being about 170,000/sq. mm. in this region.

It is interesting to note that Ramalingaswami, Leach and Sriramachari[15] found structural changes in the rods and cones and pigment epithelium of the retina in monkeys placed on a diet deficient in vitamin A. It is permitted to accept in the light of this interesting paper that, as a result of a gross vitamin-A deficiency, the retinal pigment epithelium and the visual receptors of the human eye may be similarly affected.

This is given indirect support by Hume and Krebs,[16] who showed that cone function as well as rod function was affected in a group of human volunteers deprived of vitamin A. Wald, Brown and Smith[17] showed that the carotenoid components of the rhodopsin and iodopsin systems are identical. Iodopsin is now known to be vitamin A aldehyde.

At the same time as these retinal changes occur in the posterior degenerative lesion, the choroidal vessels are equally badly hit. This is more difficult to explain. A vascular degeneration may be induced by a circulating intoxicant, as in diabetes. Clinically, the vascular changes of the degenerative lesion under discussion could be explained in the same way.

What filarial source of intoxicant might there be?

In view of the low I.D.F. in these cases and in view of the fact that in some of them no microfilariae have been found either in the skin or in the eye, microfilariae as a source are unlikely. The only other source of toxin is the adult worm. This is not outside the bounds of possibility. It has been mentioned earlier that the average number of nodule sites (nodule mean) in these cases is low (0.9), and that we found many cases without any palpable nodule, it is thus possible to argue that it is only free adult worms which permit the circulation of such a toxin. The occurrence of free adult worms has been demonstrated post mortem by van den Berghe[18] and others.

Here, too, vitamin A deficiency may play a part. The nodule mean where the posterior lesion is never seen in rain-forest villages (vitamin A being plentiful in the diet) was found by us to be 4.0 even where the density quotient was less than 5.0. Might not a deficiency of vitamin A, therefore, be in some way responsible for the low nodule mean, leaving a proportionately high number of adult worms free in the tissues?

The factors which determine the effect of the nutritional status on parasitic infestations are complex; yet Moore,[19] after reviewing the contradictory literature, suggests that the migration of parasites or of their larvae may be facilitated by defective barriers in animals deficient in vitamin A. There is some evidence for this.

It may well be that the encapsulation of adult filariae Onchocerca volvulus is to some extent determined by the vitamin-A content of the diet: the more vitamin A the greater the number of nodules; the less, the greater the number of free worms. A toxin liberated by adult worms lying free in the tissues is much more likely to achieve a reasonably high titer in the blood than if it were liberated within a comparatively avascular and densely fibrous-walled nodule. That would be one possible explanation for the absence of the degenerative lesion from rain-forest country.

If a toxin liberated by free adult worms exists, it is well known that the complexity of the choriocapillaris not infrequently results in a high local titer of any circulating poison. Owing to the huge surface area offered for absorption, retinal damage results.

How these toxic substances act is obscure, of course, and it is still debated whether all of them are essentially neurotoxic or some of them act primarily upon the choroidal or retinal blood vessels causing a secondary neuronic degeneration through vasoconstriction.

In primary choroidal sclerosis the vascular changes precede and induce the pigmentary changes, but Ramalingaswami and his colleagues did not discuss the choroidal vessels although the retinal pigment was altered as a result of vitamin A deficiency. Leach[20] says that changes in the walls of the choroidal vessels, especially the choriocapillaris, were seen in sections taken from the eyes of monkeys deficient in vitamin A in this study, but there were no changes in the retinal vessels. This may be seen in the original illustrations to the paper. Leach is the first, however, to agree that such important observations require confirmation. There is no real evidence that the vascular changes precede the pigmentary in the posterior lesion.

The degenerative lesion of onchocerciasis seems to differ from a primary choroidal sclerosis in that a vitamin-A deficiency is an ever-present factor. There is, therefore, no alternative but to postulate at least two etiologic factors. These two, of course, could be linked.

A filarial toxin may interfere in vitamin-A metabolism as well as affect the vessels. In this way a vicious circle is set up, all the more likely to appear in subjects already somewhat deficient in the vitamin. There is some evidence to support the first hypothesis.

Eveleth, Goldsby, Bolin and Bolin[21] have made preliminary studies on the conversion of carotene in sheep infested with filariform larvae after deprivation of vitamin A. A better conversion was observed in one noninfested sheep than in three which were infested. In experiments on guinea pigs, animals which were infested with D. filaria were found eight months later to have reserves averaging 2.5 i.u./gm., as compared with 23 i.u./gm. in control animals not so infested. Animals infested with D. viviparus also had lower reserves than control animals (Soliman[22]).

Several factors suggest that the pigment epithelium plays a vital role in the rod and cone degeneration. Popper and Greenberg[23] demonstrated the presence of vitamin A in this epithelium, and suggested that the vitamin is altered within it as it passes from the circulation to the receptors. Damage to the epithelium could occur secondary to a choroidal sclerosis of the type described here as being possibly induced by a filarial toxin, and would thereby lead to inhibition of the vitamin-A metabolism with a resultant adverse effect on the rods and cones; the epithelial changes, on the other hand, might be simply a primary degeneration in a vitamin-A deficient subject as a result of the generalized deficiency.

In neither of these events is it necessary to postulate a direct competitive effect by a toxin to explain the breakdown in the vitamin-A metabolism. It would be enough if the epithelium itself was made deficient in vitamin A. It is well known that the more rapid the destructive process the greater will be the deposition of retinal pigment in new locations. Everything suggests a prolonged deficiency.

In Ridley's drawing of the degenerative lesion in his monograph, and in some of the retinographs of Boithias,[24] accumulation of the retinal pigment is slight if the size of the area involved is taken into account. This supports the view that the condition is insidious and noninflammatory, which all the better fits the pathogenetic possibilities just suggested, *rather than the death of microfilariae in situ.*

To sum up, it seems likely that as a result of vitamin-A deficiency—either with or without additional interference in vitamin-A metabolism by a filarial toxin—there will be destruction of the retinal pigment epithelium which in turn will lead to degeneration of the retinal receptors. Simultaneously, a choroidal sclerosis develops, probably as the result of a filarial toxin, for it is not as yet proven that vitamin A deficiency alone can lead to

such a change. The vascular sclerosis in its turn gives a greater impetus to degeneration of the retinal pigment epithelium, thereby further aggravating the break-down in the vitamin A metabolism. The restriction of the lesion in the first instance to the papillomacular area, where the choriocapillaris is most dense, lends support to the belief that a toxin does play a part in producing the vascular changes. It should not be impossible to isolate such a toxin, if it exists. The hypothesis put foward rests partly on circumstantial evidence, but in the absence of a better argument it affords some basis on which to work in the future.

While this explanation goes as far as possible in the light of our present knowledge, it leaves us wondering why only five percent of the many subjects whose bodies almost certainly contain free adult filariae, and who are deficient in vitamin A, appear to suffer from this ocular lesion. Many might consider that five percent is a reasonable percentage in any large biologic series; others might ponder on the probability of there being a third factor involved.

In this connection, it is interesting to read of the toxin present in rye germ, the ill effects of which on the spinal cord could be prevented by vitamin A (Mellanby[25]); cereals constitute the main item of food. There are also other possibilities.

There may be some reason why the carotene which is ingested is not converted into vitamin A; the blood carotenoids were estimated in only two of our cases (1,029 and 1,291); both figures were abnormally high despite the level of vitamin A. We do not know if this is the rule; it may be an important observation, or merely misleading.

Wald and Hubbard[26] have shown that the conversion of retinene to vitamin A is a coupled reduction for which cozymase acts as a coenzyme, and fructose diphosphate can act as a substrate. The cycle is dependent on the existence of an adequate supply of nicotinic acid, which is contained in cozymase.

While there are ample amounts of nicotinic acid in the diets of the people of Northern Nigeria (Nicol[27]) there is a variable degree of deficiency in riboflavin; it is believed that a close relationship exists between these two respiratory enzyme vitamins, so that cozymase activity may well be interfered with in riboflavin deficiency. It is in directions such as these, perhaps, that further light may be thrown on this fascinating subject.

Summary

1. Two types of onchocercal lesion in the posterior uvea are shown to exist: one is due to the death of microfilariae in or adjacent to the choroid, and is inflammatory in type. The other is a degenerative lesion associated with a low degree of infection in the individual and a low nodule mean; its pathogenesis is not understood.

2. The sera from 10 cases suffering from this lesion were found to have a low vitamin-A content (about 25 i.u./100 ml. plasma). Recovery of vision (almost complete or partial in seven cases of the posterior degenerative lesion) followed the administration of 165,000 i.u. vitamin A daily. Improvement, when it occurred, began at the end of one week. In addition, the dark adaptation in early cases so treated returned to normal. There was no resolution of the anatomic abnormalities. Where atrophic cupping, peripheral corpusculation, or orange-white sclerosis of the larger choroidal blood vessels existed, no improvement resulted.

3. Assessment of possible factors in the etiology suggests that combination of vitamin-A deficiency with a toxin liberated by free adult worms could explain its onset. This belief is supported by the fact that the lesion does not occur in areas where vitamin A insufficiency in the dietary or onchocerciasis endemicity exist by themselves, but usually only when the two are associated.

Acknowledgments

Dr. H. M. Sinclair, Reader in Nutrition at Oxford University, kindly carried out the vitamin-A assays. Dr. B. M. Nicol supplied the data presented in Table 1. I am most grateful to both.

References

1. Bryant, J.: Tr. Roy. Soc. Trop. Med. Hyg., **28**:523, 1935.
2. Hissette, J.: Ann. Soc. Belge Med. Trop., **12**:433, 1932.
3. ———: "Onchocercose oculaire." Mem. Inst. roy. colon. Belge, Sci. nat., 1937, v. 5.
4. Richet, P.: Bull. Soc. Path. exot., **32**:341, 1939.
5. Ochoterena, I.: Rev. Mex. Biol., **10**:75, 1930.
6. Hughes, M. H.: (Thesis) African onchocerciasis. University of Oxford, 1949.
7. Rodger, F. C., and Brown, J. A. C.: Trans. Roy. Soc. Trop. Med. & Hyg., **51**:271, 1957.
8. Rodger, F. C.: Brit. J. Ophth., **41**:544, 1957.
9. Ridley, H.: Ocular onchocerciasis. Brit. J. Ophth. Mono., Suppl. 10, 1945.
10. Sarkies, J. W. R.: Brit. J. Ophth., **36**:81, 1952.
11. Toulant, P., and Boithias, R.: Bull. Acad. nat. Med., **136**:378, 1952.
12. Budden, F. H.: Brit. J. Ophth., **41**:214, 1957.
13. Choyce, D. P.: Tr. Roy. Soc. Trop. Med. & Hyg., **52**:112, 1958.
14. Toulant, P., Robineau, G., and Puyuelo, R.: Bull. Soc. Path. exot., **43**:615, 1950.
15. Ramalingaswami, V., Leach, E. H., and Sriramachari, S.: Quart. J. exp. Physiol., **40**:337, 1955.
16. Hume, E. M., and Krebs, H. A.: Med. Res. Coun. Spec. Rep. Ser. No. 264, 1949.
17. Wald, G., Brown, P. K., and Smith, P. H.: Fed. Proc. **11**, 304, 1952.
18. Van den Berghe, L.: Ann. Soc. belge Med. trop., **21**:261, 1941.
19. Moore, T.: Vitamin A, Amsterdam, Elsevier, London, Cleaver-Hume, 1957, pp. 481-491.
20. Leach, E. H.: Personal communication, 1957.
21. Eveleth, D. F., Goldsby, A. I., Bolin, F. M., and Bolin, D. W.: Vet. Med., **48**:441, 1953.
22. Soliman, K. N.: Brit. Vet. J., **109**:148, 1953.
23. Popper, H., and Greenberg, R.: Arch. Path., **32**:11, 1941.
24. Boithias, R.: Arch. Ophth., **14**:584, 1954.
25. Mellanby, E.: Brain, **54**:247, 1931.
26. Wald, G., and Hubbard, R.: J. gen. Physiol., **32**:367, 1949.
27. Nicol, B. M.: Brit. J. Nutrit., **10**:181, 1956.

EXTRAVASCULAR PATHWAYS OF THE EYE AND ORBIT*

PAUL R. PATEK, PH.D., AND SOL BERNICK, PH.D.

Los Angeles, California

Introduction

Whether true endothelial-lined lymphatic channels exist within the orbit has been a subject of continuous controversy and conjecture. The extent of the continuation of the subarachnoid space from the cranial cavity into the orbit is also a matter of debate and the possibility of direct communication between the subarachnoid space in the orbit with true lymphatic channels is clouded by inconsistent experimental evidence.

Tenon,[1] in 1806, described the fascia of the orbit and its communication or continuity with the meninges. He described the sheath of the optic nerve and the sclera as continuous with the dura and the continuity of the enclosed spaces with the subarachnoid space. Schwalbe,[2] in 1870, by means of subarachnoid space injections, filled the periscleral space of Tenon which he redescribed. He also described perivascular channels surrounding the vorticose veins which he said connected the periscleral space with a suprachoroidal lymphatic space. Alexander[3] described lympathics in the choroid, and Lohe[4] claimed to have seen lymphatics in the retina. Schieck[5-7] conducted experiments which led him to believe that lymph spaces surrounding the central retinal vessels communicated directly with the subarachnoid space around the optic nerve.

* From the Department of Anatomy, School of Medicine, University of Southern California. This investigation was supported by Research Grant (B-797) from the Institute of Neurological Diseases and Blindness of the National Institutes of Health, United States Public Health Service, Bethesda, Maryland.

In his studies of sclerosis of the central artery of the retina, Bridgett[8] stated that many minute spaces are present in the vascular adventitia, and he called these spaces "adventicial lymphatics." Wolff and Davies,[9] as a result of their study of experimentally induced papilledema, denied the existence of any direct extension of the perioptic nerve subarachnoid space beyond the lamina cribrosa. These authors also believed that any spaces so described were the result of excessive injection pressures or were caused by the use of permeable injection masses.

More recently, Nishimura[10] injected either India-ink or silver nitrate into the cranial subarachnoid space in rabbits. He described the resultant spread of the injected materials into the subarachnoid space around the optic nerve and into the suprachoroidal lymph space as far anterior as the ora serrata. He also described communicating endothelial-lined lymphatics in the areas of the vorticose veins and the annulus tendineus. These lymphatics he concluded were related to the orbital muscles and the retrobulbar fat. Nishimura also described a continuation of the subarachnoid space along the central vessels of the retina, in one instance extending as far as the papilla.

Materials and Methods

A. Extensions of the subarachnoid space

To demonstrate the perioptic nerve subarachnoid space and its possible extension, the method used by Patek[11] to demonstrate the perivascular spaces of the brain was used. The technique, a modification of that used by Weed and McKibben[12] and Weed,[13] involved an intravenous injection of hypertonic sodium chloride solution to increase the osmotic pressure of the blood and thus dehydrate the tissues. Simultaneously, a suspension of colloidal mercury sulfide in physiologic salt solution was allowed to replace the osmotically withdrawn cerebrospinal fluid. It was assumed that dehydration of orbital tissues, as well as the reduction of intraocular pressure (Davson and Thomassen,[14] and Duke-Elder and Duke-Elder[15]), would cause a flow of cerebrospinal fluid containing the colored suspension through the subarachnoid space into the orbit and thus outline its normal anatomic pathways within the orbit. In this manner the artefacts produced by pressure injection into the subarachnoid space (Wolff and Davies[9]) would be avoided.

The experimental animals were cats and rabbits. The animals were anesthetized by Nembutal and ether. A small trephine opening two mm. in diameter was made in the parietal eminence with a dental bur. A hypodermic needle was inserted through the dura and arachnoid into the subarachnoid space. Another needle was inserted into the femoral vein in the cat or, into the ear vein in the rabbit. Six to eight cc. of 30-percent sodium chloride were slowly injected intravenously and two to four cc. of colloidal mercury sulfide were allowed to enter the subarachnoid space under atmospheric pressure. Eighty minutes following the beginning of the experiment the animal was killed, and the entire orbit was removed and fixed in alcoholic Bouin's solution. The blocks of tissue were decalcified in 10-percent nitric acid in 10-percent formalin and embedded in celloidin. The embedded blocks were sectioned at 20 to 100 micra. The cut sections of cat's eyes were usually treated with potassium permanganate and oxalic acid in order to bleach the pigment, and then stained by hematoxylin and eosin and mounted, or mounted unstained.

B. Lymphatic vessels

In order to demonstrate the possible presence of true lymphatics the "indirect" or "puncture" type of injection was made in the living animal anesthetized with Nembutal and ether. The injection mass, either India-ink (Higgins) or colloidal mercury sulfide suspended in physiologic salt solution, was injected slowly and under minimal pressure through a 27-gauge hypodermic needle. Multiple injections of 0.5 cc. to 0.2

cc. of the colloidal suspension were made into all parts of the eyeball, the extrinsic muscles and the orbital fat and connective tissue. The animals were then killed, and the entire orbit was removed and fixed in alcoholic Bouin's solution. In several animals, before any tissues were removed, the common carotid artery was exposed and cannulated, and the blood vessels were first perfused with physiologic saline, and then filled with Ranvier's Prussian blue solution. This latter procedure was carried out to eliminate the confusion between blood vessels and lymphatics of the eye. The removed tissues were treated in a manner similar to that previously described.

Observations

A. Extensions of the subarachnoid space

Recognition of the extension of the intracranial subarachnoid space around the optic nerve was facilitated by the injected material, colloidal mercury sulfide, plus the histologic characteristics of the mesothelial cells which line the subarachnoid space. The lining of this channel was continuous with the pia and arachnoid membranes of the cranial cavity and was found to continue uninterruptedly as a sleeve surrounding the optic nerve. Just proximal to the lamina cribrosa the pia and arachnoid became continuous, obliterating the enclosed space (fig. 1).

Within the cranial cavity the mesothelial cell lining of the subarachnoid space, functioning as macrophages, ingested colloidal mercury sulfide particles. This phenomenon was not seen in the perioptic nerve extension of pia and arachnoid. As in the cranial cavity, many fine trabeculae traversed this extension of the subarachnoid space (fig. 1).

These trabeculae were formed by mesothelial cells and usually surrounded a core of fine connective tissue fibers. At the sites of entrance of the central retinal vessels into the optic nerve only a slight pouching of the pia surrounding these vessels was discernible. In no instance were the injected particles seen in relation to the central vessels of the

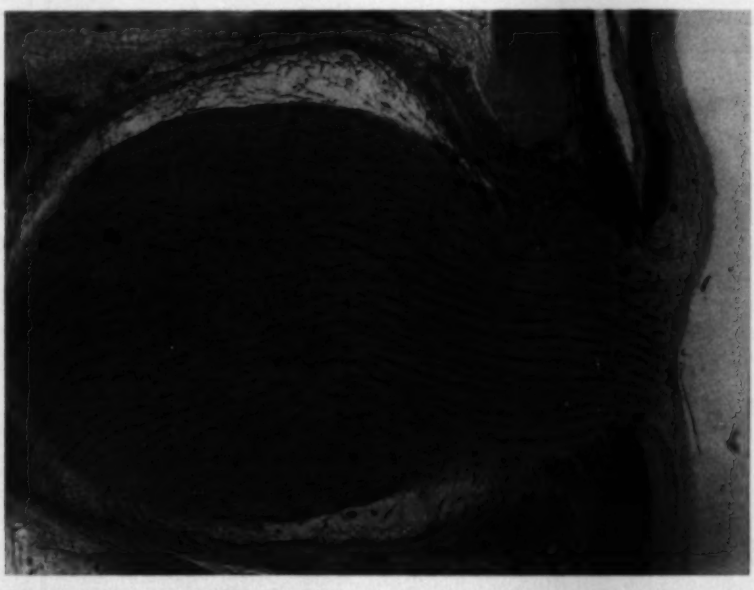


Fig. 1 (Patek and Bernick). The perioptic nerve extension of the subarachnoid space and its fine trabeculae are lightly outlined by the contained colloidal mercury sulfide particles which cling to the pia and arachnoid. (Cat, hematoxylin and eosin, ×35.)

retina beyond their point of entrance into the optic nerve.

B. Lymphatic vessels

At the points of injection of the India-ink or colloidal mercury sulfide, this colored substance completely surrounded the structural elements of the area and obliterated them from view. From these localized areas the material spread into the surrounding tissues and in some instances into ruptured blood vessels. Thick cleared sections showed that streamers of the colored substance had permeated loose connective tissue. The looser the binding connective tissue, the greater was the distance of spread from the site of injection. The vascular perfusion by a differently colored suspension showed that the vessels which contained colloidal mercury sulfide were blood vessels and not lymphatic vessels.

In no instance were true endothelial-lined lymphatic vessels observed. When thin sections were studied, injected spaces seemed to possess definite boundaries and appeared similar to lymphatics. Thick sections, however, showed these spaces to be thin connective tissue planes cut in cross-section. In all specimens the potential spaces injected were found to be areas of loose connective tissue or planes between loosely adherent more dense tissues. The potential spaces injected may be conceived as circulatory channels but they can not be called lymphatic vessels. No lymphatic vessels were found in relation to or draining these clefts or spaces and the spaces did not communicate with the perioptic nerve subarachnoid space.

In the extraocular tissues of the orbit there was little resistance to the dispersion of the injected material. The dye followed the paths of loose connective tissue around the extrinsic muscles of the eye and between fat lobules. Within these muscles this material was dispersed between muscle fiber bundles. Within the episcleral or periscleral cleft the injected material was widely dispersed within the loosely bound tissues.

Within the eyeball, the suprachoroid layer of the choroid allowed the greatest spread of the suspension (fig. 2). Here the injected material could be traced as an almost continuous lamina from the area around the lamina cribrosa into the base of the ciliary body (fig. 3). The foreign particles surrounded the fibrous and cellular elements

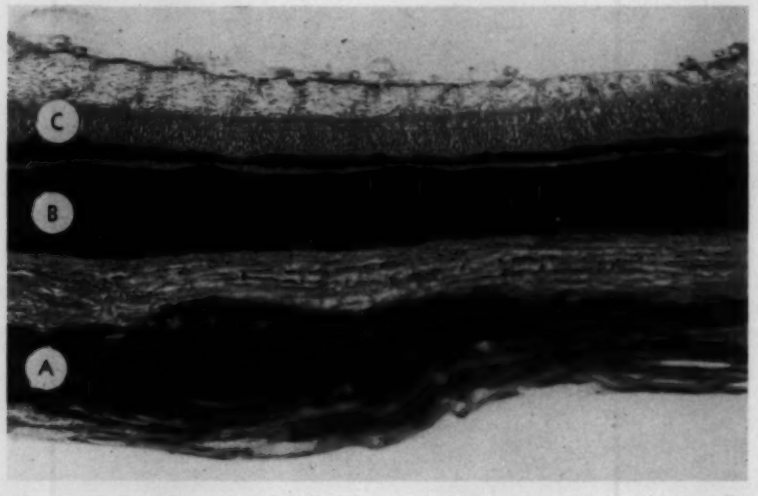


Fig. 2 (Patek and Bernick). Injected India-ink has penetrated between the collagenous fiber bundles of the sclera (A), spread within and distended the suprachoroidal layer of the choroid (B) and fills the cleft between the pigment cells and rods and cones of the retina (C). (Cat, hematoxylin and eosin, ×125.)

Fig. 3 (Patek and Bernick). Injected India-ink within the suprachoroidal layer of the choroid (B) spreads anteriorly as far as the base of the ciliary body. (Cat, hematoxylin and eosin, ×75.)

of the suprachoroidal tissue. No injected particles had passed from this potential space into the perioptic nerve subarachnoid space. The vascular layer of the choroid allowed only a limited spread of the foreign substance between blood vessels and within the adventitia of some of its blood vessels. In the retina, a small amount of the injected material was located as a thin layer between the rods and cones and the pigment epithelium (fig. 2). Only individual particles had permeated the tissues surrounding the retinal nerve fibers and blood vessels. The dense connective tissue of the sclera limited the excursion of the injected substance in this layer of the eye (fig. 2). and in the cornea the foreign particles were seen between the lamellae of collagenous fibrils in a small area surrounding the point of injection.

Discussion

In order to discuss properly the various circulatory channels of the eye and orbit it becomes necessary first to clarify terms. Unfortunately the earlier literature, for the most part, does not discriminate between the terms lymph, tissue fluid and cerebrospinal fluid, nor between the spaces which contain these fluids. With the possible exception of the intraocular chambers, all spaces are referred to as lymph spaces or lymphatics, without regard to the distinction between endothelial-lined lymphatic vessels, loose connective tissue cleavage planes or mesothelial-lined extensions of the intracranial subarachnoid space.

If a cannula or hypodermic needle is plunged blindly into the optic or perioptic tissues, and an injection mass is forced into these tissues, as is the procedure in the direct injection method for the demonstration of lymphatics, the result will be a spreading of the injection mass within loose connective tissue surrounding blood vessels, nerves, muscles, and between layers of more dense substances. It will also fill any ruptured blood or lymphatic vessels of the area. The injected substance which is under the pressure of the injection as well as that of the displaced tissues will, without doubt, be forced along the pathways of least resistance.

In order to differentiate the possibly injected spaces or vessels, it is necessary to distinguish each by its morphologic characteristics. To aid in this differentiation, it is advisable to perfuse the blood vessels with an injection mass of a color different from

that used in the puncture injections. Also it is advisable to prepare thick (at least 100 micron) cleared sections in addition to the usual thin sections in order to differentiate the more gross morphologic patterns of blood vessels, lymphatic vessels and tissue clefts, since it is often extremely difficult to distinguish them by their cellular structure alone.

Injections of colored substances into the subarachnoid space surrounding the optic nerve when made with too great a pressure will rupture the lining pia-arachnoid membrane and permeate the surrounding tissues. Those substances which escape from this mesothelial-cell lined space will follow the loose connective tissue pathways of least resistance. Also, substances permeable to the pia-arachnoid membrane will escape its confines and may lead to erroneous conclusions.

This series of experiments confirms the findings of Wolff and Davies.[9] These authors described the perioptic nerve subarachnoid space as an extension of the intercranial subarachnoid space which continues anteriorly only as far as the lamina cribrosa and there terminates as a closed channel. The described extensions of this space by Schwalbe[2] must, therefore, be the result of rupture or diffusion through the mesothelial cell membrane and the subsequent flow of injected substances along connective tissue cleavage planes. Therefore, the periscleral, perichoroidal or suprachoroidal and perivascular spaces of Schwalbe are loose connective tissue spaces and not extensions of the subarachnoid space. Because these spaces of Schwalbe are, in effect, loose connective tissue spaces, they cannot be called lymphatics or lymph spaces.

The lymphatics described by Alexander,[3] Lohe,[4] Leboucq,[16] Bridgett[8] and others, are either descriptions of blood vessels or connective tissue clefts, or, their use of the terms lymphatics and lymph spaces included tissue fluid spaces, which is not in agreement with our current definition of these words. Although connective tissue spaces or clefts may not be termed lymphatic vessels or lymph spaces, their significance as circulatory mechanisms of the eye cannot be denied. In several animals (rabbits), Evans' blue dye (T-1824) was injected into the anterior chamber. Cleared sections showed that the dye not only diffused into the regional scleral veins, but was also traced for some distance within the suprachoroidal space.

In conclusion it may be stated that no true endothelial-lined lymphatics are present within the orbit except for the lids and conjunctiva; and that the perioptic extension of the subarachnoid space as a mesothelial-lined channel extends into the orbit only as far as the lamina cribrosa. A number of loose connective tissue clefts containing tissue fluid are present. These clefts do not communicate with any lymphatic vessels nor are they continuous with the perioptic nerve subarachnoid space. What role these tissue fluid clefts may have in the circulatory mechanisms of the eye needs further study.

University Park (7).

References

1. Tenon, J. R.: Observations anatomiques sur quelques parties de l'oeil. Paris, 1806.
2. Schwalbe, G.: Untersuchungen über die Lymphbahnen des Auges und ihre Begrenziengen. Arch. f. mikr. Anat., **4**:1-61, 261-262, 1870.
3. Alexander, A.: Ueber die Lymphkapillaren der Choroidea. Arch. f. Anat. & Physiol., Anat. Abst., 1889, pp. 117-122.
4. Lohe, W.: Uebe sichtbare Lymphbahnen der Retina. München, Kestner and Lessen, 1902, pp. 1-13.
5. Schieck, F.: Die Genese der Stanungspapille. Weisbaden, Bergmann, 1910.
6. ———: Beitrage zur Kenntniss der Genese der Stauungspapille. Arch. f. Ophth., **78**:1-48, 1911.
7. ———: Ueber die Verbindung der perivasculären Räume im Axailstrange mit dem Zwischenscheidenraum des Opticus. Arch. f. Ophth., **113**:157-159, 1924.
8. Bridgett, C. R.: Sclerosis of central artery of retina. Am. J. Ophth., **9**:725-735, 1936.
9. Wolff, E., and Davis, F.: A contribution to the pathology of papilloedema. Brit. J. Ophth., **15**:609-632, 1931.
10. Nishimura, S.: Extravasculäre Softbahnen des Augapfels and Sehnerven und ihre Beziehung zu den orbitalen Lymphgafässen. Acta Sch. Med. Univ. Kiota, **31**:121-130, 1953.

11. Patek, P. R.: The perivascular spaces of the mammalian brain. Anat. Rec., **88**:1-24, 1944.
12. Weed, L. H. and McKibben, P. S.: Pressure changes in the cerebrospinal fluid following intravenous injections of solutions of various concentrations. Amer. J. Physiol., **48**:512-530, 1919.
13. Weed, L. H.: The absorbtion of cerebrospinal fluid into the venous system. Am. J. Anat., **31**: 191-221, 1923.
14. Davson, H., and Thomassen, T. L.: The effect of intravenous infusion of hypertonic saline on intraocular pressure. Brit. J. Ophth., **34**:355-359, 1950.
15. Duke-Elder, P. M., and Duke-Elder, W. S.: Studies on the intraocular pressure: II. The physiochemical factors controlling the intraocular pressure. J. Physiol., **71**:268-274, 1931.
16. Leboucq, M.: Some experiments concerning the lymph vessels of the eye and the orbit. (Translated by A. Alt) Am. J. Ophth., **30**:225-232, 1913.

SHORTENING OF THE ANGLE OF THE ANTERIOR CHAMBER IN ANGLE-CLOSURE GLAUCOMA*

GEORGE GORIN, M.D.
New York

The purpose of this paper is to describe an atypical mode of closure of the angle frequently observed in chronic noncongestive angle-closure glaucoma. Instead of the angle closing first at its entrance, as is the rule in an attack of angle-closure glaucoma, the closure begins at the periphery and advances toward the line of Schwalbe. The closure consists of a permanent progressive fusion between the root of the iris and the trabeculae overlying the canal of Schlemm. Gonioscopically, this obliteration of the peripheral part of the angle results in a characteristic appearance which may be described as "shortening of the angle" (fig. 1).

GONIOSCOPIC APPEARANCE

In a typical case of angle-closure glaucoma the angle closes during an attack of elevation of intraocular pressure and opens again when the tension returns to normal. In the cases of angle-closure glaucoma which are associated with a shortening of the angle, the anterior part of the trabecular band remains visible even though the tension is elevated. Gonioscopically, this type of angle may be erroneously regarded as open and may thus lead to a diagnosis of chronic simple glaucoma. It is evident that the success of treatment depends on a correct interpretation of the gonioscopic findings. If the angle closure mechanism is responsible for the elevation of tension, an iridectomy is the operation of choice; if, on the other hand, one is dealing with a narrow, but open angle, as in chronic simple glaucoma, an iridectomy cannot be expected to control the tension.

By gonioscopic criteria, an angle is considered open when the entire width of the trabecular band, including the scleral spur, is visible. Unless the scleral spur is visible one cannot be sure that one sees the whole trabecular band. Under certain circumstances, however, the angle may still be considered open to drainage even when no part of the trabecular band is visible. This is the case when the periphery of the iris is ballooned forward so as to conceal the anterior wall of the angle.

That an open space exists between the periphery of the iris and the anterior wall of the angle may be presumed from the displacement of the focal lines reflected from the posterior surface of the cornea and the anterior surface of the iris (fig. 2). When, on the other hand, the angle is shortened by obliteration of its periphery, it may be closed to drainage even when the anterior part of the trabecular band is visible. For, it is through the posterior two thirds of the trabeculae, namely those adjacent to the canal of Schlemm (functional trabeculae) that drainage of aqueous takes place; these are blocked either partly or entirely by fusion of the peripheral angle structures.

* From the Department of Ophthalmology, Albert Einstein College of Medicine, Yeshiva University, and the Glaucoma Clinic of the Manhattan Eye, Ear and Throat Hospital.

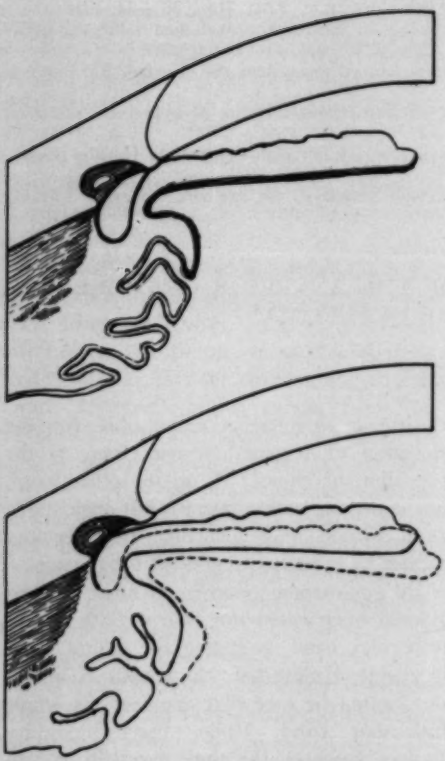


Fig. 1 (Gorin). (Upper) Closure of the angle at its entrance by contact between the periphery of the iris and the line of Schwalbe. (Lower) Shortening of the angle by fusion between the root of the iris and the posterior part of the trabecular band (functional trabeculae). The entrance to the angle remains patent but drainage of aqueous is blocked. Dotted lines show position of iris before closure of angle. Solid lines show position of iris after closure.

Illustrative case reports

The following cases illustrate the essential differences in modes of closure of the angle in the typical and atypical varieties of angle-closure glaucoma.

Case 1

Closure of the entrance to the angle in acute congestive glaucoma in the right eye. Very narrow entrance to the angle without elevation of tension in the left eye.

C. S., a 56-year-old woman, was seen for the first time in January, 1957, with an attack of acute congestive angle-closure glaucoma in the right eye of one week's duration. Tension was 65 mm. Hg (Schiøtz), the cornea was steamy and epithelial bullae were present. The pupil was dilated and vision was limited to light perception. The iris showed areas of necrosis on the temporal and nasal sides of the pupil and there was a three-plus flare in the aqueous.

She was treated with a retrobulbar injection of two cc. of procaine with hydase and adrenalin, was given 1000 mg. of Diamox orally and frequent instillations of 2.0 percent pilocarpine and 2.5 percent hydrocortone. After five hours of treatment the tension was 40 mm. Hg. The cornea was then cleared a bit with glycerine and the angle was found completely closed on gonioscopic examination.

As the patient refused to have an iridectomy done immediately, she was maintained on 2.0 percent pilocarpine, 2.5 percent hydrocortone and Diamox. After three days the tension was 25 mm. Hg but the cornea remained cloudy and the angle closed. The following day, the tension rose again to 65 mm. Hg and could no longer be controlled with Diamox.

A basal and complete iridectomy was done ab externo on the 13th day after the initial attack. The postoperative course was uneventful; the cornea cleared after three days and the tension has remained normal since then. Postoperative gonioscopy showed the angle open and a wide band of trabeculae covered with pigment was visible.

The left eye of this patient has a shallow chamber and the periphery of the iris is ballooned forward, making it impossible to see the landmarks of the anterior wall of the angle. There is, however, considerable displacement of the focal lines and the tension has always remained normal. The patient is using 2.0 percent pilocarpine solution in the left eye every three hours. She was advised to have a prophylactic iridectomy in the left eye, but refused

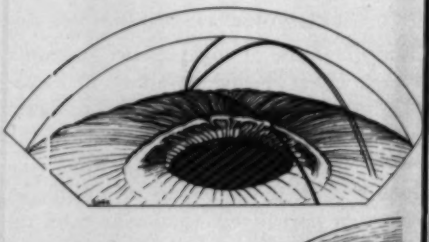


Fig. 2 (Gorin). Gonioscopic appearance of very narrow but open angle. None of the structures of the anterior wall are visible. Note the displacement of the focal lines reflected from the posterior surface of the cornea and the anterior surface of the iris.

surgery. Vision in both eyes is correctible to 20/20 and tension is 22 mm. Hg.

CASE 2

Shortening of the angle of the anterior chamber by progressive obliteration of its peripheral part in chronic noncongestive angle-closure glaucoma with mild elevations of tension. Forward creeping anterior peripheral synechias.

M. L., a 37-year-old woman, was first seen in May, 1957, with a history of mild elevations of tension for the past two years. Vision was 20/20 in each eye. The discs and fields were normal. Tension was 40 mm. Hg, without miotics.

On gonioscopic examination, the whole trabecular band was visible in some parts of the angle, while in others only the anterior part of it was seen. There were anterior peripheral synechias between the root of the iris and the posterior trabeculae (functional trabeculae). The synechias apparently formed slowly and their creeping progression toward the line of Schwalbe accounted for the uneven obliteration of the periphery of the angle. The anterior chamber was of intermediate depth in the axial and midperipheral portions; in the periphery there was abrupt narrowing of the chamber and the iris appeared angulated and not ballooned as in a typical case of angle-closure glaucoma.

Treatment with pilocarpine (2.0 percent) solution every three hours lowered the tension to 22 mm. Hg in the right eye and 25 mm. Hg in the left eye. In November, 1957, the tension climbed up to 25 mm. Hg in the right eye and 35 mm. Hg in the left eye in spite of the constant use of miotics. Gonioscopic examination at that time showed that the angle remained the same as before in the right eye. In the left eye, the anterior peripheral synechias appeared to be advancing toward the line of Schwalbe.

In January, 1958, a basal iridectomy was performed on the left eye. Since the operation tension is maintained at 22 mm. Hg in the left eye. Without miotics the tension is 30 mm. Hg. Gonioscopically, the anterior peripheral synechias which were present before the operation remained the same, while the open parts of the angle became wider and the whole trabecular band is seen there.

CASE 3

Shortening of the angle of the anterior chamber by progressive obliteration of its peripheral part in chronic noncongestive angle-closure glaucoma. Intermittent acute elevations of intraocular pressure by massive contact between the root of the iris and the functional trabeculae. Anterior part of trabeculae visible gonioscopically in the presence of high tension.

F. S., a 50-year-old woman was first seen in April, 1958. She had vague complaints about her eyes, none of which suggested glaucoma. Tension was 55 mm. Hg (Schiøtz) in both eyes. Vision was 20/25 in each eye, discs normal, no cupping. The anterior chamber was of intermediate depth in the axial and midperipheral portions.

Gonioscopic examination showed abrupt shallowing of the chamber periphery near the entrance to the angle, where the iris was angulated. The anterior portion of the trabecular band was visible. There was little displacement of the focal lines indicating that there was contact between the root of the iris and the posterior, invisible, part of the trabeculae.

The patient was given 2.0 percent pilocarpine solution to be used every three hours. With this treatment the tension was maintained at 30 mm. Hg in each eye. After stopping the drops for 24 hours in preparation for a dark-room test, the tension rose to 65 mm. Hg in both eyes. In spite of the high tension there was no corneal edema or pain.

On gonioscopic examination the anterior third of the trabecular band was visible. The dark-room test was not done and the patient was instructed to resume treatment with pilocarpine. When seen the following day the tension was 40 mm. Hg in both eyes. The anterior half of the trabecular band was visible gonioscopically.

In order to determine whether one was dealing with an open-angle glaucoma or with the angle-closure mechanism it was decided to do the mydriasis test. One drop of Neosynephrine (10 percent) was instilled into the left eye. The pupil dilated promptly, the tension remained 40 mm. Hg after 30 minutes and the angle showed no change. After one hour, however, the tension rose to 90 mm. Hg and gonioscopic examination showed that the angle was completely closed. The periphery of the iris was plastered against the posterior surface of the cornea. It took eight hours of intensive treatment, which consisted of a retrobulbar injection of procaine, oral administration of 1250 mg. of Diamox, and repeated instillations of pilocarpine (2.0 percent) and eserine (0.5 percent) to bring the tension down to 25 mm. Hg.

At that time there was no doubt that one was dealing with an angle-closure glaucoma, in which closure was atypical. It began in the peripheral part of the angle and progressed toward the line of Schwalbe. This explained why the entrance to the angle was still open in the presence of a tension of 65 mm. Hg.

A basal and complete iridectomy was performed on the left eye on June 11th and on the right eye on June 17th. The postoperative course was uneventful. At present both eyes show an open angle. The whole width of the trabecular band is visible but there is little displacement of the focal lines, indicating that the periphery of the angle is closed. The patient has a mild residual glaucoma, the tension being 25 mm. Hg in both eyes with miotics and 35 mm. Hg without miotics.

COMMENT

In a typical case of angle-closure glaucoma the angle closes by contact between the periphery of the iris and either the line of Schwalbe or the posterior surface of the cornea in front of the line of Schwalbe. In such eyes only the entrance to the angle is

blocked in the early stage, while the rest of the angle may remain normal, with a normal trabecular meshwork behind the line of contact. If closure of the entrance is allowed to persist, there follows progressive obliteration of the peripheral part of the angle by contact between the root of the iris and the trabecular meshwork. This mode of closure occurs during an acute attack of elevated tension in eyes with uniformly shallow chambers and extreme forward bowing of the periphery of the iris.

Gonioscopic examination reveals in the normotensive periods between attacks a very narrow, slitlike entrance to the angle and considerable displacement of the focal lines (fig. 2). When the entrance to the angle closes, the tension rises and the anterior wall of the angle cannot be seen on gonioscopic examination. The focal lines are not displaced; on the contrary, they are continuous and form a geometric angle, the apex of which corresponds to the point of contact between the anterior and posterior walls of the chamber angle (fig. 3). This mode of closure of the angle is seen both in congestive attacks of angle-closure glaucoma and during attacks of high tension in some cases of noncongestive angle-closure glaucoma.

In many cases of noncongestive angle-closure glaucoma, however, the angle closes first in the peripheral part. This results in a characteristic gonioscopic appearance: the angle is shortened owing to obliteration of its peripheral zone, while the entrance to the angle remains open (fig. 4). It may be assumed that some unknown pathologic process produces fusion which commences in the periphery and results in synechias between the posterior part of the trabeculae and the root of the iris.

These synechias advance slowly toward the line of Schwalbe and can be seen gonioscopically in various stages of development. In the early stage there is fusion only between the root of the iris and the posterior part of the functional trabeculae, causing slight impairment of outflow and mild elevations of intraocular pressure. The greater part of the functional trabeculae remain accessible to drainage and tension is controlled with miotics.

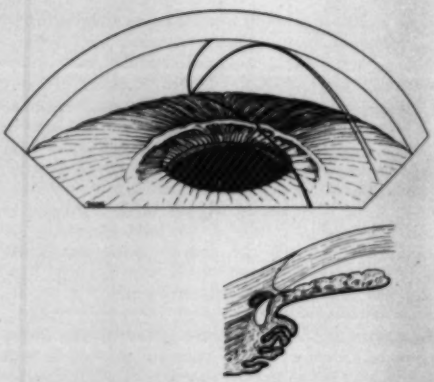


Fig. 3 (Gorin). (Upper) Gonioscopic appearance of a closed angle. Periphery of the iris is bowed forward. The focal lines form a geometric angle the apex of which corresponds to the point of fusion between the periphery of the iris and the line of Schwalbe. (Lower) Closure of the angle at its entrance.

The rate of progression of the synechias varies in different parts of the angle. In some sectors the synechias are ciliary, that is, there is fusion between the root of the iris and ciliary body. In other sectors the synechias advance toward the sclera spur and midtrabecular area. In still others, they reach the anterior part of the trabecular band and even the line of Schwalbe.

This slow forward creeping of the synechias causes uneven obliteration and shortening of the periphery of the angle. In the advanced stage, as more and more of the functional trabeculae become blocked by synechias, the tension rises to high levels. The pupil is slightly dilated and miotics have little effect because the root of the iris is bound down to the functional trabeculae by massive anterior peripheral synechias.

Gonioscopically, however, the anterior part of the trabecular band is still visible and the entrance to the angle remains patent. At this stage it is possible to diagnose shortening of the angle by the appearance of the focal lines in the optic section of the angle. The focal line reflected from the visible part of the trabeculae is continuous with the focal line reflected from the periphery of the iris.

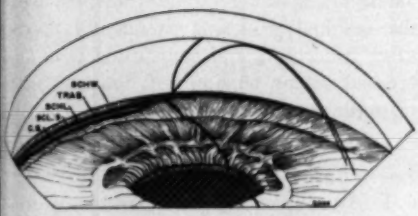


Fig. 4 (Gorin). Gonioscopic appearance of a shortened angle. Peripheral parts of the angle are unevenly obliterated by forward creeping synechias in various stages of development. On the extreme left side the angle is open. The trabecular band, scleral spur, and ciliary body are visible. In the center, the anterior peripheral synechia advanced to the scleral spur and midtrabecular area. On the extreme right a broad-based synechia advanced to the line of Schwalbe.

The absence of displacement of the focal lines indicates that there is fusion between the root of the iris and the functional trabeculae. (fig. 5).

In some cases contact between the root of the iris and the functional trabeculae takes place in the greater part of the angle circumference. This massive obliteration of the periphery of the angle accounts for the very high intermittent elevations of tension (Case 3). The contact may be reversible in the early stages, but becomes permanent and irreversible in the late stages of the disease.

Differential diagnosis

Shortening of the angle is an atypical mode of closure observed in noncongestive angle-closure glaucoma in eyes in which the axial and midperipheral portions of the anterior chamber are of intermediate depth. The chamber becomes shallow abruptly in the periphery (fig. 5). Forward ballooning of the iris periphery, so characteristic of the average case of angle-closure glaucoma, is absent or minimal; instead, the iris is angulated, running a horizontal course at the entrance to the angle and assuming a nearly vertical position in the midperiphery of the chamber.

In the incipient stages of shortening of the angle, chronic noncongestive angle-closure glaucoma may be confused with chronic simple glaucoma. Problems in differential diagnosis arise chiefly from the fact that a noncongestive clinical course is common to both types of glaucoma. Impairment of outflow in both conditions sets in gradually and tensions are only moderately elevated. Also, the gonioscopic appearance of a shortened angle, in which the anterior part of the trabecular band is visible, may be misinterpreted as an open angle.

In order to detect shortening of the angle, careful and repeated comparative gonioscopic studies should be undertaken. A decrease in displacement of the focal lines combined with an increase in tension are usually sufficient to put one on guard against the possibility of closure of the periphery of the angle. Also the appearance of synechias creeping forward toward the line of Schwalbe is helpful in making a diagnosis. The darkroom and mydriasis tests may be helpful in making a differential diagnosis between this

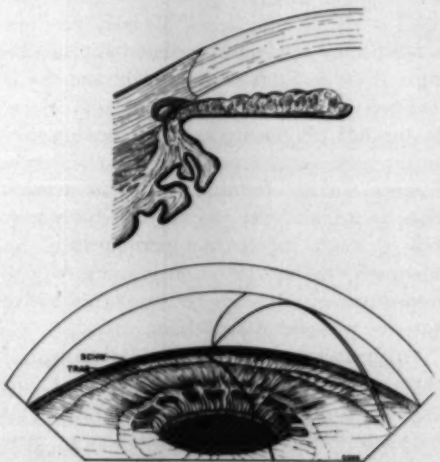


Fig. 5 (Gorin). (Upper) Shortening of the angle by fusion between the posterior portion of the trabecular meshwork (functional trabeculae) and the iris root. Only the anterior portion of the trabecular meshwork remains free. The angle is closed to drainage although the entrance remains open. (Lower) Gonioscopic appearance of a uniformly shortened angle. The periphery of the iris is angulated. The entrance to the angle is open and the anterior portion of the trabecular band is visible in the presence of high intraocular pressure. There is no displacement of the focal lines, indicating that the invisible peripheral part of the angle is obliterated.

atypical form of noncongestive angle-closure glaucoma and simple glaucoma. The darkroom test is of value only when positive, but is inconclusive when negative. The mydriasis test presents a certain amount of risk. When the functional trabeculae are already blocked nearly all around the circumference, dilatation of the pupil may precipitate an acute congestive attack by pushing the iris against the anterior wall of the angle and blocking outflow completely (Case 3).

Treatment

It is important to diagnose obliteration of the periphery of the angle in the incipient stage because it is in this stage that the glaucoma is most amenable to treatment by iridectomy.

When a diagnosis of shortening of the angle is made, an iridectomy should be performed without delay even though the tension is only slightly elevated (Case 2). The fact that the anterior part of the trabecular band is visible gonioscopically may give one a false sense of assurance that complete closure of the angle is not imminent and one is inclined to delay surgical treatment. Delay in surgical treatment results in gradual closure of the angle around the entire circumference. In the terminal stage the tension rises to a high level and an iridectomy may fail to lower the tension permanently. An adequate filtering operation is more difficult to perform at this stage because of extensive anterior peripheral synechias.

An iridectomy done in the early stage of closure of the angle usually normalizes the tension. It prevents further progression of incipient synechias and formation of new ones. Gonioscopic examination after iridectomy reveals that the parts of the angle which were open prior to surgery become wider, while those which were closed by synechias remain unchanged.

It is often necessary to use miotics postoperatively in order to maintain the tension at normal levels, since even the free trabeculae have undergone pathologic changes as a result of recurrent contact with the iris. These changes are probably responsible for the residual glaucoma frequently observed after iridectomy and manifested both by increased ocular tension and lowered facility of outflow.

Summary and Conclusions

1. An atypical mode of closure of the angle frequently encountered in noncongestive angle-closure glaucoma is described. This closure consists of obliteration of the peripheral parts of the angle by anterior peripheral synechias, which advance from the periphery of the angle toward the line of Schwalbe. Fusion between the root of the iris and the functional trabeculae results in a characteristic gonioscopic appearance which may be termed "shortening of the angle."

2. Shortening* of the angle is to be differentiated from closure of the angle at the entrance which is typical in acute congestive attacks of angle-closure glaucoma and in some cases of noncongestive angle-closure glaucoma during periods of elevation of tension.

3. Three cases are presented to illustrate the essential differences between typical closure of the angle at its entrance and atypical closure by shortening of the angle through obliteration of its peripheral parts.

4. Shortening of the angle results in a gonioscopic appearance which is difficult to interpret. The chronic noncongestive course and the patency of the entrance to the angle make the differential diagnosis between some cases of noncongestive angle-closure glaucoma and simple glaucoma a difficult clinical problem.

5. An early iridectomy is recommended in angle-closure glaucoma, in which the angle is shortened.

585 West End Avenue (24).

---

* After this paper was completed for publication a paper by Dr. Julius Kessler was published in the December, 1958, issue of The American Journal of Ophthalmology dealing with the same two mechanisms of closure of the angle (A discussion of the mechanisms in chronic angle-closure glaucoma, 46:888, 1958).

NOTES, CASES, INSTRUMENTS

ESSENTIAL ATROPHY OF THE IRIS

WITH THE REPORT OF AN UNSUCCESSFUL ATTEMPT TO PREVENT GLAUCOMA BY EARLY IRIDECTOMY

SAMUEL TRACY CLARKE, M.D.
Reno, Nevada

CASE REPORT

Mrs. F. R. P. was first seen on January 23, 1953. Examination revealed a normal 44-year-old, white woman with no history of any disease or injury which might affect the eyes, except that for three years she had noticed slight pain and discomfort in the right eye. Vision in each eye was 20/20 without correction. Fields, tension, and muscle balance were all normal. The left eye was completely normal by fundus and slitlamp examination, but the right eye showed the pupil slightly drawn-up toward the 1-o'clock position, with essential iris atrophy and there were several areas above and below the deformity where the iris stroma was atrophic. Gonioscopy revealed an anterior synechia at the point of deformity and another area at the 12-o'clock position. The remainder of the angle was open.

A complete medical survey was done and the only abnormality was a gold sol curve of 112,220,000 in the spinal fluid.

The iris atrophy progressed rapidly and trial steroid therapy, both local and general, was of no benefit. The question of doing a large basal iridectomy to prevent glaucoma was discussed with the patient. Consultation was held with Dr. A. E. Maumanee who concurred with the diagnosis but was not willing to advise surgery because of the risks involved, and because the tension had always been normal. Another gold sol curve on November 27, 1953, showed 0,111,100,000.

The anterior synechias increased rapidly and by June, 1954, a large basal iridectomy was done in hope of preventing glaucoma by leaving at least part of the angle open below. There were no complications, and by January, 1957, no iris substance was visible. Fields and tension remained normal and at least two thirds of the iris angle was closed with scar tissue from atrophied iris.

On April 7, 1958, the patient, four years after iridectomy, had tension, of 36 mm. Hg., but fields were normal and there were no changes on the disc. Up to the present time the use of DFP and Diamox has barely controlled the tension, but there are no field changes and the lower one fourth of the angle is open. The other eye is completely normal.

CONCLUSION

A large basal iridectomy failed to prevent or cure the glaucoma in essential iris atrophy, even though it was done over almost a quarter of the angle before the development of anterior synechias. Whether the appearance of glaucoma four years later was delayed by the operation, and whether future control of the tension will be made easier by the salvage of part of the open angle is a mute point. The question of whether complete removal of the iris in the early stages of this disease would have prevented glaucoma is another matter and should be considered in relation to the increased danger of such drastic surgery versus the known danger of glaucoma.

130 North Virginia Street.

TEST FOR CENTRAL SEROUS RETINOPATHY

BASED ON CLINICAL OBSERVATIONS AND TRIAL

HARRY MAGDER, M.D.
Montreal, Quebec

Flat detachment of the retina, central angiospastic retinitis, retinitis centralis annularis, and central serous retinopathy are among the terms given to a condition affecting the macula, especially in men between the ages of 30 and 50 years who are physically fatigued and are under some emotional stress. The term central serous retinopathy will be used in this paper.

Symptomatically there is a sudden disturbance of vision with such complaints as positive scotoma, micropsia, metamorphopsia, or that objects have an amber hue. The condition usually lasts several weeks but clears up eventually and all or most of the complaints disappear.

On examination the fundus reveals, in advanced cases, an area of edema surrounding the fovea, so that there is an elevation of the retina, seen with the ophthalmoscope or the slitlamp. There is usually a ring-shaped light reflex surrounding the macula

and, in some cases, the elevation seems to have a pale, pinkish background. After repeated attacks the macular area often assumes a granular appearance and seems peppered with fine pigment. Recurrences are common and usually one eye is affected at a time.

No treatment currently used has seemed to have any immediate effect on the course of the disease. Therapy has included large doses of corticosteroids orally, cessation of smoking, the use of Diamox or vasodilators. In one recent case I used forced oxygen inhalation, with no improvement.

Klien[1] differentiates three varieties of this condition and classifies them as (a) those which indicate a process limited to the retina, (b) those in which participation of the choroid must be assumed from the beginning, (c) those in which the choroid appears to be, at least from the beginning, the only part affected.

Gifford and Marquardt[2] studied a series of cases and were able to show that central serous retinopathy was associated with an abnormal state of the autonomic nervous system.

The observation I am about to describe was first made by me in December, 1954. I have not seen it reported elsewhere.

A patient who had been diagnosed as having central serous retinopathy on three previous occasions called saying that he had another attack. His first attack was in his left eye, starting in December, 1949, with recovery in May, 1950. There was recurrence in the left eye with typical macular findings in October, 1951. This attack cleared up quickly but was followed in November, 1951, with an attack in his right eye that lasted eight weeks. As soon as the right eye cleared, he complained that the left eye was blurred and that the symptoms were the same as on all previous occasions.

On checking his visual acuity it was found to be 20/20 in each eye. I examined the fundi but could not see any signs that suggested a fresh attack of central serous retinopathy, and told him so. He appeared puzzled. He closed his right eye and complained that the vision of his left eye was very blurred now. I again checked his visual acuity and found that it had dropped to 20/6 in the left eye but that the right one was normal. After an interval he noted that there was recovery of vision. The examination of each fundus was repeated, and the same results occurred, normal vision in the right eye but a drop in the acuity of the left eye, with recovery after an interval.

From that time on I used this test in all cases with lesions of the macula in order to determine if it would hold good for other macular diseases. The test is performed as follows:

In all cases of suspected disease of the macula the visual acuity is taken with a manifest refraction performed to obtain the best vision. This is necessary as many of the more advanced cases develop considerable hyperopia with edema of the macula. Then the macula of the right eye is studied with the light of the ophthalmoscope for 15 seconds (an arbitrary figure) and the visual acuity is again noted and a check made of time of recovery of the visual acuity to its level before the test was done, that is, before the light was focussed on the fovea. The test is then repeated on the left eye. If the eye is normal, vision recovers in 15 to 60 seconds. In central serous retinopathy, delay of recovery of central vision may last an hour or more. In severe cases vision may drop from 20/20 to 20/200 and slowly improve line by line. I have tested patients with macular changes due to diabetic and hypertensive retinopathy, central choroiditis, senile degeneration, and various other conditions and in none of these is the test positive.

One case of central serous retinopathy was particularly interesting.

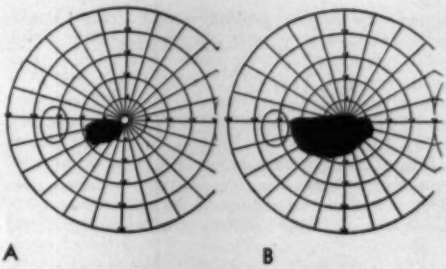
A woman, aged 44 years, was first seen for routine refraction in June, 1951. She was emmetropic and had 20/20 vision in each eye. In Octo

1955, she complained of blurred vision of the left eye. With a +1.75D. sph. vision in that eye was 20/20. Vision in the right eye was normal with no correction. On examination I noted that there was marked edema about the macula of the left eye. Recovery time was 20/40 in 20 minutes and 20/25—in one hour. Recovery time of the nonaffected eye was 20 seconds. In February, 1956, she accepted no sphere and had 20/20 vision. Recovery time was 45 seconds. I saw her in December, 1958, for a routine check up and recovery time of each eye was 30 seconds.

After it was concluded that this test was specific for edema of the macular area, I began to search for an explanation. A short paragraph in Adler[3] *Clinical Physiology of the Eye* suggested an article by Lange and Simon,[4] who found that when retinas of carp were placed in Ringer's solution and exposed to light, the solution became acidified by phosphoric acid. This did not occur when retinas in Ringer's solution were kept in darkness. They found that the acid appeared when the pigment epithelium was attached to the neuroepithelium and that *no* acid appeared when there was *no* pigment epithelium in contact with the neuroepithelial layer. They were also able to demonstrate that when the two retinal layers were in contact, repeated exposure to light caused repeated formation of acid. If only pigment epithelium were used, no acid appeared.

If we accept these observations to mean that, with separation of the two layers of the retina, there is loss of normal recovery of retinal function after exposure to light, then the mechanism by which my test works in central serous retinopathy can be explained as follows:

When the macula is exposed to the light of the ophthalmoscope, a chemical reaction occurs which requires that the two layers of the retina be in contact in order for normal recovery of retinal function to take place when the light is removed. In central serous retinopathy, however, there is actual separation of the two retinal layers in the macular area, making it possible for this test to differentiate this condition from other lesions in, in front, or behind the macula in which there is



A B

Fig. 1 (Magder). Left eye of patient, M. R. W. (A) Central field with Lloyd stereocampimeter, one-mm. white, after full recovery. (B) Same patient re-examined.

no separation of the two layers of retina. These would include malignant melanoma, early central choroiditis, disciform degeneration of the macula, and so on. Because some cases of central serous retinopathy have been mistakenly diagnosed as retrobulbar neuritis, probably due to multiple sclerosis, every suspected disturbance of central vision should have the benefit of this simple test. A positive test suggests a favorable prognosis and repeated testing helps in plotting the progress of the disease.

Case report

Mr. W., aged 48 years, complained that his left eye was bothering him. He said that everything he looked at had a yellowish color and that, if he looked at a light and then away from it, a spot appeared in his line of vision. He also said that he had a similar attack in his right eye a year ago and although it recovered, lines still appear distorted when viewed with it.

During this patient's previous attack, his oculist reported that vision in the right eye was 20/40 during the attack but cleared up to 20/25 following recovery. Vision in his left eye was 20/20 at that time and there was no delay in recovery time. The oculist, who was familiar with the test herein reported found it was positive in the right eye at that time but not in the left.

On recurrence, March 7, 1959, external examination showed the eyes to be normal. Pupillary reflexes were normal. Examination of the right fundus showed the media to be clear. The disc and vessels were perfectly normal. Although no sharp foveal reflex was noted, there was no apparent edema of the macula. Recovery time after foveal illumination was 45 seconds.

The left fundus also had clear media and normal disc and blood vessels. However, the macular area

showed the swelling typically seen in central serous retinopathy, with a wide surrounding light reflex ring. Just temporal to the fovea there was a pinkish oval elevation. Following the light test, Mr. W.'s vision dropped to less than 20/200 with recovery to 20/80 in four minutes and to 20/40 in 10 minutes.

On full recovery his central fields were plotted using a Lloyd stereocampimeter. With a one mm. test object there was a paracentral scotoma (fig. 1A). After re-examination of the fovea the scotoma became much larger and was now centroparacentral (fig. 1B).

This is the patient on whom I used forced inhalations of oxygen to see if they would influence the recovery time. I found that they did not.

Summary

1. A test that might be useful in the clinical examination of patients has been described.

2. The test consists of recording the time of recovery of central vision following exposure of the fovea to the light of the ophthalmoscope.

3. An explanation for the physiologic mechanism involved has been suggested.

2122 Crescent Street.

References

1. Klien, B. A.: Macular lesions of vascular origin. Am. J. Ophth., **36**:1, 1953.
2. Gifford, S. R., and Marquardt, G.: Central angiospastic retinopathy. Arch. Ophth., **21**:211, 1939.
3. Adler, F. H.: Clinical Physiology of the Eye. New York, Macmillan, 1933.
4. Lange and Simon: Ztschr. Phys. Chem., **120**:1, 1922.

DIFFERENTIAL DIAGNOSIS OF AN EDEMATOUS OPTIC DISC

Charles H. Howarth, M.D.

and

William H. Havener, M.D.

Columbus, Ohio

The importance of a differential diagnosis in the presence of an edematous optic disc is evident when one considers that the diagnosis of optic neuritis may prevent subjecting the patient to expensive, traumatic, and sometimes hazardous neurosurgical diagnostic procedures. The impression that good visual acuity excludes the diagnosis of optic neuritis is not valid. Chamlin (1953) reported 100 cases of optic neuritis, in 21 percent of which there was retention of good visual acuity.

It is in early cases that optic neuritis (intraocular) and papilledema cannot be readily differentiated, for the fundus findings in these two conditions closely resemble one another. Ophthalmoscopic differentiation is, therefore, impossible. Perimetry is a valuable diagnostic aid, and the demonstration of a central, paracentral, cecocentral or arcuate scotoma, coupled with a history of sudden onset of visual loss, is diagnostic of optic neuritis. Since enlargement of the blindspot is caused by both conditions, it does not aid diagnosis. Diagnosis is aided by the presence of orbital pain, and it is the purpose of this paper to present data which indicate that recognition of the inflammatory characteristics of optic neuritis will aid in its clinical differentiation from papilledema.

In 1935 Selinger reported that the albumin content of the aqueous in papilledema was 0.02 percent or lower; that in optic neuritis varied from 0.04 to 0.10 percent. With these data in mind, Chamlin (1959) reported his observations on the slitlamp examination of patients with papilledema and optic neuritis. He specifically looked for products of inflammation in the aqueous and found no aqueous flare or floaters in 24 patients with papilledema. However, in four patients with optic neuritis, aqueous flare and floaters were present. Admitting his series to be small, Chamlin felt, however, that his findings were important in the differential diagnosis of optic neuritis and papilledema. He believed the inflammatory products reached the aqueous through the vitreous, although he made no comments on the vitreous findings. Chamlin stated that there seemed to be no mention of these diagnostic criteria in the literature.

TABLE 1
SUMMARY OF CASES

	Number of Eyes	Cases with Cells in Anterior Vitreous
Papilledema	40	0
Optic neuritis	13	9

TABLE 2
DIFFERENTIAL DIAGNOSTIC CRITERIA

	Spontaneous Venous Pulsation		Ability to Collapse Veins with External Pressure	
	Yes	No	Yes	No
Papilledema	4	32	33	5
Optic Neuritis	3	10	13	0

PRESENT STUDY

For some time it has been the custom at our clinic to use the biomicroscope to differentiate between papilledema and optic neuritis by recognition of cells in the anterior vitreous, which is easily examined through a dilated pupil. Although inflammatory products undoubtedly originate at the optic nerve, it is technically difficult to recognize cells in the posterior vitreous.

As the data in Table 1 indicate, cells were not found in the anterior vitreous in 40 cases of papilledema, but were present in nine of 13 cases of optic neuritis. However, absence of cells in the vitreous does not rule out optic neuritis, for no cells may be exhibited if the edema is due to an inflammatory lesion posterior to the disc. Disc edema alone does not produce cells in the vitreous.

An incidental but interesting and practical finding is presented in Table 2. The presence or absence of spontaneous venous pulsation or the ability to collapse the central retinal vein with external pressure is of no help in differentiating optic neuritis from papilledema. It has been said that the inability to collapse the veins by external ocular pressure indicates papilledema. This is a reasonable statement which is, however, often reversed to state that papilledema is not present if the veins will collapse—which is *not* true.

University Hospital (10).

REFERENCES

Chamlin, M.: Visual field changes in optic neuritis. Arch. Ophth., **50**:699-713, 1953.
——: Aqueous floaters in the differential diagnosis of papillitis and papilledema. Arch. Ophth., **61**: 744, 1959.
Havener, W. H.: Differential diagnosis of papilledema. Ohio State M. J., **51**:1096, 1955.
Selinger, E.: Choked disc and papillitis. Arch. Neurol. & Psychiat., **33**:360-367, 1935.

BULBAR SUBCONJUNCTIVAL EPITHELIAL CYST*

ROBERT D. BROWNELL,† M.D.
Ann Arbor, Michigan

Subconjunctival epithelial cysts are commonly seen by the eye pathologist. They occur as a result of either trauma or chronic inflammation. The traumatic cysts are most often formed by subconjunctival inclusion of epithelium which results in cyst formation. In chronic inflammation epithelial downgrowth or the approximation of epithelial folds may result in cyst formation. These cysts characteristically have a basement membrane surrounded by a layer of connective tissue containing small blood vessels. This results in some degree of fixation to the surrounding tissue layers, and necessitates dissection in order to accomplish removal.

This case is reported because it is felt to be unusual in several respects.

* From the Department of Ophthalmic Surgery of the University of Michigan Medical Center, Ann Arbor, Michigan.
† Senior Medical Student, University of Michigan.

Fig. 1 (Brownell). Artist's conception of the subconjunctival cyst in the left eye of the patient.

Case report

On December 2, 1958, a 60-year-old white woman came to the Ophthalmology Clinic of the University of Michigan Medical Center. She stated that she had first noticed a swelling in her left eye in August, 1958. No history of trauma or inflammation could be elicited. The patient had no other ophthalmologic complaints, but did exhibit slight lagophthalmos, O.U., from previous thyrotoxicosis.

Figure 1 illustrates the appearance of the lesion. On examination it was noted that the swelling was a translucent cystic ovoid mass about 3.0 by 2.0 by 2.0 mm. The nodule appeared free of any attachment to the bulbar conjunctiva, subconjunctival connective tissue, or sclera for it could be moved about easily beneath the conjunctiva.

The eye was anesthetized with two-percent Xylocaine and a small incision was made over the mass. The cyst spontaneously emerged through the incision.

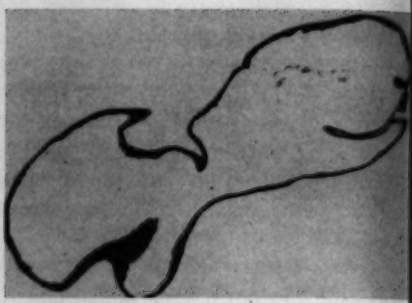


Fig. 2 (Brownell). Low-power view of a hist logic section of the removed cyst, the wall of whi is composed of epithelium only. (Hematoxylin-eos stain, photomicrograph.)

Microscopic examination revealed a cystic stru ture lined by several layers of nonkeratinized e thelium, hyperplastic in certain areas, with an int basement membrane. The cavity was empty exc for a few areas of homogeneous material wh stained a faint blue. The patho-anatomic diagno was conjunctival inclusion cyst. Figures 2 and represent photomicrographs of a typical section.

Comment

The cyst described is believed unique the following respects:

1. The absence of any connective tiss or vascular elements around the cyst.
2. The absence of any attachment of t cyst to the surrounding tissue layers.
3. The absence of a history of previo trauma or inflammation.

Fig. 3 (Brownell). High-power view of the epithelial wall of the cyst which exhibits a distinctly vi basement membrane (arrow). (Hematoxylin-eosin stain, photomicrograph.)

The ability of the relatively large cyst described in this case to remain viable without any vascular supply was considered particularly unusual. Apparently nutrition was derived solely from tissue fluids.

University Hospital.

A DACRYOCYSTORHINOSTOMY NEEDLE*

J. G. F. Worst, M.D.
Groningen, The Netherlands

The suturing device as illustrated in Figure 1 serves for the purpose of suturing in a confined space as, for instance, when uniting the nasal mucosa to the lacrimal sac or when performing certain otorhinolaryngological operations.

Construction

The actual needle has a coaxially spiralled shape. It carries its eye on the tip. From the eye a dorsal groove runs the whole length of the curvature of the needle and a smaller ventral groove continues only a few mm. The needle is permanently fixed to an exchangeable conical holder which is screwed to the pencil-like shaft. The terminal knob closing the shaft also serves as a key for tightening the needle-cone. For this purpose it carries a central pin, fitting in a small hole in the cone. The needle must be threaded from the outside inward and the central part of the thread must not be tight but should run to the bobbin with a loop.

Application

When suturing, the needle is held like a pencil and is made to penetrate the tissue (or two flaps of tissue, as the case may be) by simply imparting a rotating movement to it. When the needle tip emerges from the tissue, the central part of the thread will lie protected in the dorsal groove, but the peripheral part of it will leave the small ventral groove, geometrically speaking, forming a chord to the curvature of the needle. Consequently it is automatically ready for drawing through. Obviously it is this peripheral part that should be drawn through, as taking the central part would unthread the needle.

For greater ease a special crotchet is provided for this manipulation. The thread is simply hooked on with it and the needle is withdrawn by rotating it in the reverse direction. The whole operation is performed in a few seconds and is far easier than the de-

*From the University Eye Clinic.

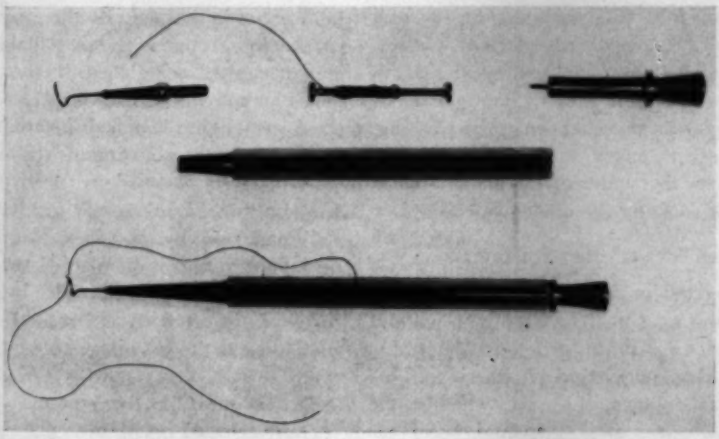


Fig. 1 (Worst). The dacryocystorhinostomy needle.

scription suggests. The thread is knotted and if preferred the knot can be tightened by sliding the eye of the needle onto it. After cutting, the needle still holds the thread, ready for the next suture, while the bobbin makes reloading during surgery unnecessary.

It would seem that this instrument† solves the specific difficulties which arise in deep suturing.

v. Starkenborghstraat 10.

† This instrument is manufactured by K. Otter, Medische Instrumentmakerij. van Imhoffstraat 3, Groningen, Holland, for whose ingenious help I am grateful.

A FOUR-WAY SIGHT SCREENER

EMANUEL KRIMSKY, M.D.
Brooklyn, New York

This plastic elongated figure-of-eight bar made of plexiglass consists of four separate components which enable the examiner to perform four separate eye screening tests without having to rely on four separate units. These components include: (1) a bull's eye pinhole; (2) a translucent red "glass"; (3) a maddox rod; (4) an occluder.

1. THE BULL'S EYE PINHOLE

The pinhole "disc" consists of a blackened circular area with a central opening $\frac{1}{32}$ inch in diameter. It is used to ascertain whether sight could be improved by eyeglasses in those whose vision is poor without glasses or with the glasses they happen to be wearing. The subject is asked to look through the bull's eye, or the center of the black circular area, while keeping the other eye covered.

2. THE RED "GLASS" TEST FOR DIPLOPIA

In suspected or alleged diplopia one first inspects the eyes with a flashlight without using a red glass in order to determine whether there is deviation of either eye. This is done as follows: (1) see whether the corneal light reflex is displaced from the normal or central pupillary position in suspected deviating eye; and (2) see whether the eyes move alternately as the subject is asked to look first at one "light" and then at the other. Because a red glass can create an awareness of seeing double in those who have no true diplopia one should proceed as follows in testing for diplopia:

A. Make a preliminary inspection of the eyes without a red glass, using only a flashlight for near and a 75-watt lamp for far. When there is binocular diplopia one should always find deviation in one eye as well as displacement of the corneal light reflex in the affected eye. A temporal or outward displacement of the corneal light reflex indicates convergent strabismus. When the eye turns out the corneal light reflex is displaced inward from the center of the pupil.

B. If the subject contends he sees two "lights" instruct him to look first at one "light" and then at the other. Alternate fixation or movement of the eyes is now observed and this confirms any suspicion that binocular diplopia is real.

C. Place the red glass before either eye preferably the fixing eye. This results in seeing a red and a white image. Have the subject keep looking at the red image seen behind the red glass. This enables the examiner to concentrate on the uncovered deviating eye and to study the displacement of the corneal light reflex in that eye. By the position of the corneal light reflex in this deviated eye the examiner can tell at a glance whether the diplopia is homonymous or crossed or vertical. If the corneal light reflex is displaced outward or temporal, as in convergent strabismus, the false image is likewise projected outward or temporal or homonymously in relation to the red image seen by the fellow eye. If the corneal light reflex is displaced inward, as in divergent strabismus, the false or secondary image is projected inward or nasal or crossed in relation to the red image seen by the fellow eye.

D. To measure the amount of diplopia for any selected position or distance of gaze operate a graded prism (rotary prism

prism rack) over the uncovered deviating eye until the displaced corneal light reflex is restored to a normal or central pupillary position (prism reflex test). During this change in prism strength the red and white images will at the same time come together. This simple objective test not only provides a measurement of the amount of diplopia and ocular deviation, but also confirmatory objective proof of the existence of diplopia.

3. The maddox rod component

The maddox rod consists of cylindrical shaped translucent rods each about three mm. in diameter. Looking at a test light through any of these rods produces a linear streak image at right angles to the axis of the rod itself. In testing for phoria in those having supposedly straight eyes the rod is first placed in a horizontal axis before either eye to yield a vertical line of light seen through that eye while the uncovered eye sees the true image of the test light at the same time. In orthophoria the two images are superimposed. In esophoria or exophoria the two images are separated and are arranged homonymously in esophoria and crossed in exophoria. The method of measuring for heterophoria (latent strabismus) with the maddox rod over one eye and prism over the other is fully explained in Army manuals and in textbooks on the eye.

In a manifest strabismus where there is no spontaneous diplopia one can, using the maddox rod, also induce double images artificially the same as in straight eyes having heterophoria, unless visual suppression is marked. These induced image responses will indicate whether there is normal or abnormal retinal correspondence. The term "retinal correspondence" points to an abnormal binocular visual state which one finds in every case of chronic manifest strabismus where one uses only one eye at a time and sees single. Normal retinal correspondence simply means that the relative positions of the two images created by using the maddox rod conforms to the law of normal retinal projection the same as in esophoria or exophoria,

Fig. 1 (Krimsky). The four-way sight screener. (a) Maddox rod. (b) Red filter. (c) Pinhole disc. (d) Occluder.

or as in a paralytic strabismus with spontaneous diplopia.

A procedure to follow in examining for retinal correspondence with the maddox rod in manifest strabismus is as follows:

A. First ascertain whether there is a true strabismus by using an ordinary flashlight. In manifest strabismus the corneal light reflex will be displaced in a direction opposite to that of the eye deviation. For example, in convergent strabismus the corneal light

reflex will be displaced outward or temporal from the center of the pupil.

B. Rule out the existence of spontaneous diplopia as the subject is instructed to look at a test light with or without the aid of a red glass, as the case may require. Because diplopia is already present there is no longer need to create it with the maddox rod.

C. If the person sees single, aim to create double images by placing the maddox rod horizontally before either eye, preferably the fixing eye, in order to test for horizontal strabismus, convergent or divergent. Except in marked visual suppression the subject will see two images simultaneously, a vertical streak image seen with the fixing eye and a true image of the test light seen with the uncovered eye. The relative positions of these two images in relation to the deviation of the eyes will determine whether one is dealing with a normal or an abnormal retinal correspondence. When the induced double images are homonymous and correspond to a known amount of convergent strabismus, then the retinal correspondence is said to be normal because it follows the law of normal retinal projection. In spontaneous binocular diplopia projection of the false image also follows the same law. When the diplopia induced by the maddox rod in a known case of convergent strabismus is crossed rather than homonymous, retinal correspondence is said to be abnormal rather than normal because it does not conform to the law of normal retinal projection.

D. One can also measure the amount of normal or abnormal retinal correspondence in manifest strabismus as follows:

a. Measure the amount of ocular deviation by ascertaining the amount of prism required to restore the displaced corneal light reflex to a central or normal pupillary position, and supplement this with a cover test to see that motion of the eyes is stopped.

b. Place the maddox rod horizontally before the fixing eye to create a vertical streak image. Have the subject keep looking at the streak image in order to study the deviation in the uncovered eye. A graded prism, such as a prism rack or a rotary prism, is now placed before the uncovered eye and moved until the corneal light reflex is restored to a central or normal pupillary position, and eye movement is stopped on alternate fixation of the streak image and the test light image. If, as a result of prism, the images are superimposed then retinal coresponding is said to be normal. The image readings must correspond to the deviation readings. Any appreciable differences point to abnormal retinal correspondence and these are noted accordingly.

745 Eastern Parkway (13).

References

Krimsky, E.: The Management of Binocular Imbalance. Philadelphia, Lea, 1948, pp. 177-180.

———: Method of objective investigation of strabismus. J.A.M.A., **145**:539-544 (Feb.) 1951.

War Dept.: Notes on Eye, Ear, Nose and Throat in Aviation Medicine. Technical Manual No. 8-30[illegible] Washington, D.C., Nov. 26, 1940, p. 122.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*
700 North Michigan Avenue, Chicago 11

ALAN C. WOODS, *Consulting Editor*
Johns Hopkins Hospital, Baltimore 5

BERNARD BECKER
640 South Kingshighway, Saint Louis 10

WILLIAM L. BENEDICT
15 Second Street, S.W., Rochester, Minnesota

FREDERICK C. CORDES
384 Post Street, San Francisco 8

SIR STEWART DUKE-ELDER
63 Harley Street, London, W.1

EDWIN B. DUNPHY
243 Charles Street, Boston 14

F. HERBERT HAESSLER
561 North 15th Street, Milwaukee 3

PARKER HEATH
Sullivan Harbor, Maine

S. RODMAN IRVINE
9730 Wilshire Boulevard,
Beverly Hills, California

BERTHA A. KLIEN
950 East 59th Street, Chicago 37

JAMES E. LEBENSOHN
4010 West Madison Street, Chicago 24

DONALD J. LYLE
411 Oak Street, Cincinnati 19

WILLIAM A. MANN
251 East Chicago Avenue, Chicago 11

A. EDWARD MAUMENEE
Johns Hopkins Hospital, Baltimore 5

P. ROBB MCDONALD
Lankenau Medical Building, Philadelphia 31

FRANK W. NEWELL
950 East 59th Street, Chicago 37

JOHN V. V. NICHOLLS
1414 Drummond Street, Montreal

ALGERNON B. REESE
73 East 71st Street, New York 21

PHILLIPS THYGESON
220 Meridian Road
San Jose 26, California

KATHERINE FERGUSON CHALKLEY, *Manuscript Editor*
Lake Geneva, Wisconsin

Directors: WILLIAM L. BENEDICT, President; FREDERICK C. CORDES, Vice-President; WILLIAM A. MANN, Secretary and Treasurer; ALGERNON B. REESE, DERRICK VAIL, ALAN C. WOODS.

Address original papers, other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 700 North Michigan Avenue, Chicago 11, Illinois;* Society Proceedings to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in *double space,* with wide margins.

Exchange copies of the medical journals should be sent to *Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.*

Subscriptions, application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 664 North Michigan Avenue, Chicago 11, Illinois.* Copy of advertisements must be sent to the manager by the 10th of the month preceding its appearance.

Change of address notice should be received not later than the 10th of the month prior to the issue for which the change is to go into effect. Both old and new addresses should be given.

Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Fifty reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Company, Inc., Curtis Reed Plaza, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

LIMITED VISION

One of the most satisfying experiences granted to us as ophthalmologists is the opportunity to make a patient again able to see. This experience is made more vivid when the patient has been under the impression that there was no way of making him again able to see and thus he sought no aid. And the same experience is flavored further in another dimension when the patient has been regularly under the care of capable physicians or agencies and no attempt has been made to raise his vision with other than ordinary spectacles or to refer him to a clinic where such work is done. Surely, there is need for clarification. These problems are not only related to patients and doctors but to the workers with the blind as well.

Let us consider each category: First, the ophthalmologist. It is common-place knowledge that the majority of eye physicians do not work with low-vision aids. A principal reason is that it is the general impression that to do this work requires special and unusual skill. This assumption, however, is not true. Every ophthalmologist by virtue of his training *can* participate, and by his participation more people who can be helped can be reached. Inroads to solving this problem are being made by the concerted efforts of an ever-increasing number of physicians.

Education also demonstrates that expensive equipment is not necessary. In the past few years there have been a number of articles written on low vision testing, and all publications make the point of emphasizing that equipment need not be complicated, and skill is within the realm of any eye doctor. All one needs is the "will to help."

A second category includes persons who come in contact with the visually handicapped. They must be made aware that each afflicted person is entitled to a re-evaluation of his ocular situation. Too often, an unfavorable diagnosis made years ago is permitted to condemn a patient forever. It has been found that in a significant number of cases a careful refraction done with a fresh approach may offer much. It is up to the worker who has contact with such patients to arrange for check-ups. The patient resigned to his loss may not have access to such information.

Another point needing clarification is the attitude regarding use of the eyes. It was once held that people who had poor vision should not use their eyes more than absolutely necessary. The influence was that poor sight meant "weak eyes"—a term fortunately rarely heard now—and weak eyes became worse by reading. Therefore, to conserve the eyes one must be careful. And careful meant large print so as not to *strain* the eyes.

This very suggestive concept of *weak eyes* and *eye strain* has little basis in fact. The terms explain everything and yet nothing. Like the diagnosis of "torpidity of the liver," a "cold in my back," they locate a discomfort and give a seemingly sound explanation —but they are not valid.

Eyes do not become weaker through use. In fact, reading is a skill that improves with use. It is normal and natural for a poor-sighted person and even a normal-sighted person who reads little or not at all to be uncomfortable when he again uses his eyes for this task. Surely, each succeeding week he will read better and better and more comfortable with practice; and the smaller type he learns to read, the easier will the average type be.

Sight-saving classes originally subscribed to the idea of larger type and more learning with the other senses than the eye. And it may seem inconceivable to dedicated teachers in this field to accept the present concept. This does not mean that their work has been in vain. Rather their efforts brought progress in better care, and, as more is learned, adjustments in philosophy become part of that progress. Twenty-five years ago it was incredible to think of getting a patient with a major operation out of bed within 24 hours; now it is unthinkable to keep him in bed for a week or two, as was former practice.

The child with poor vision is now being integrated more and more into regular classes. He is supported, when necessary, with visual aids and special books. An interesting observation, sufficiently repeated, warrants this next statement. Many children with very poor vision learn to read as quickly as those better sighted. It seems that this accomplishment feeds the ego of such a child, who probably reasons that here he has done with poor eye sight what his neighbor has done with normal eyes. Therefore, "if I had normal eyes, I'd do still better—I must be good." This assumption urges further education accomplishment and more often than not these youngsters are in the upper third of their classes. One suspects that education does not involve the eyes as much as has been believed. If the child with poor vision, wh

can be helped with a visual aid, after being given the opportunity of going to regular school, doesn't succeed, there is time enough for special classes.

Now, a few thoughts regarding the patient. In general, young persons do better than the older ones. Reading through an aid requires a technique different from ordinary reading. For one thing, the field of vision is smaller—less words are encompassed by the eye and one has to read in a mosaic pattern by piecing words together. This is not difficult but does require patience and practice and encouragement.

An Occupational Therapy Department is very helpful in guiding the patient through these early orientations. The patient must want to see—too many give lip service to the desire for sight but prefer to use this handicap to camouflage their greater desire for attention and unwillingness to accept responsibilities which recovered sight may threaten.

The patient must be realistic in his expectation from a device. He cannot walk wearing a strong telescope, he cannot read at an arm's length from the eye, his glasses have to look different and at times are conspicious. The patient must realize that poor vision is not a crime of which to be ashamed; and special devices to help them are no symbols of shame and dishonor.

One can expect many old persons to require visual aids. Their use will permit many oldsters to enjoy life in spite of a degenerative eye condition. It is well to remember that old age may be likened to a model-T Ford—one cannot expect a smooth ride but one can be grateful that there is transportation. To be able to grow old counting the blessings rather than the blows is better than any retirement plan.

In regard to the actual visual aids themselves: there are many and they increase each month. They have different names, cost varying amounts of dollars, and they all resolve themselves into diopters. Thus, when it is determined that so many diopters are needed, one has recourse to many devices.

The ophthalmologist truly desiring to help his patient to see will add to his armamentarium the few simple devices necessary to do this work and not leave his responsibility unfulfilled.

Albert E. Sloane.

SCIENTIFIC EXHIBITS

The exhibits at the American Academy of Ophthalmology and Otolaryngology have long been one of its outstanding features. In recent years the scientific exhibits have improved a great deal in presentation of the material and in the quality of the work presented. At the meeting last October, there were a total of 28 scientific exhibits, 15 of which related to ophthalmology.

In an effort to stimulate more and better exhibits, the academy each year awards three prizes to the outstanding exhibits in ophthalmology and otorhinolaryngology. The determination of these awards is based upon three factors of equal value. The first factor is the originality of the work presented; the second consideration is the teaching value of the exhibit; and, finally, the method of display of the material presented. The awards, based on the above factors, are made by a committee of three, one of whom is a layman associated with the display industry. Obviously, in presenting these awards, the American Academy of Ophthalmology and Otolaryngology in no way expresses an endorsement or approval of the material presented or the opinions expressed in the exhibit.

The 15 recent exhibits in ophthalmology can be roughly divided into two groups; those of purely educational value presented by organizations interested in ophthalmology, and those primarily of scientific interest.

There were a number in the first group. Dr. Charles Sheard presented an exhibit explaining the functions and work of the American Board of Opticianry and Education Foundation in Ophthalmic Optics. New Eyes for the Needy, Inc., a nonprofit volunteer organization told of its work in provid-

ing glasses and artificial eyes for needy individuals. The exhibit of Dr. Maurice Hart and his co-workers presented the textbooks for the visually handicapped as provided by Aid To Visually Handicapped. The Seeing Eye, Inc., told of their work in the field of the seeing eye dog, while the exhibit of the American Foundation for the Blind presented the problem of the individual in whom blindness occurs after the age of 40 years. The National Society for the Prevention of Blindness analyzed the diagnostic data on approximately 6,000 children attending schools and classes for the blind, with emphasis on the relative importance of the various causes of blindness.

The purely scientific exhibits were of particular interest and of high caliber. Dr. H. Richard Blackwell and his co-workers presented psychophysiologic data obtained on patients with heredodegenerative conditions of the retina. This study included such conditions as complete and incomplete achromatopsia and retinitis pigmentosa.

One of the most interesting presentations was that of Dr. Edward Okun on retinal tears in eyes examined at autopsy. In this group of eyes, fundus photographs demonstrated retinal tears undiagnosed during life. These photographs were accompanied by photomicrographs of the histologic findings in these cases. The clinicopathologic study of the cornea by Drs. Lorenz Zimmmerman, Sam T. Jones, and William F. Hughes was based on corneal buttons removed from patients at the time of keratoplasty. This made it possible to correlate the clinical features of certain corneal diseases with the histopathologic alterations found in the excised corneal tissue. The studies of Drs. Helen Chi, Miguel Martinez, and C. C. Teng dealt with: (1) the repair of endothelium, (2) the reaction of full-thickness corneas to various preservatives, and (3) the lytic effect of the aqueous on collagen fibers that have been exposed, due to a defect in the normal cellular covering.

Dr. DuPont Guerry, III, and his associates presented a modification of the anterior chamber lens together with the experimental development of the lens and instruments for the operation in this still experimental field of surgery. The presentation of Dr. Dan M. Gordon dealt with the use of the corticosteroids in the therapy of uveitis. Dr. Gilbert Baum and Mr. Ivan Greenwood demonstrated the application of ultrasonic locating techniques to intraocular and intraorbital pathologic changes. This included such conditions as retinal detachments, tumors, vitreous hemorrhages, radiolucent foreign bodies in light-opaque eyes, and in orbital tumors.

The exhibit of the American Association of Orthoptic Technicians dealt with the use of diplopia in orthoptics, demonstrating the various ways to overcome suppression and the recurrence of squint by the use of diplopia.

From the above résumé of the scientific exhibits, it seems apparent that the ophthalmologist in a short time can learn what lay organizations interested in ophthalmology are doing. Much of this work is in fields where ophthalmologic conditions make outside help necessary. By being familiar with the work of these organizations, we can be helpful to our patients.

A study of the scientific exhibits makes it possible to be aware of some of the clinical and laboratory research that is taking place at our eye centers. A discussion with the exhibitor will often bring out some diagnostic or therapeutic feature that is very helpful in everyday practice.

The ophthalmologist who fails to visit the scientific exhibits is not taking advantage of one of the ever increasingly outstanding features of the academy meeting.

Frederick C. Cordes.

NEW RESEARCH LABORATORY

Of the Wills Eye Hospital

The Wills Eye Hospital has been caring for the ocularly ill for more than 126 years. During that time millions of patients have been attended by the staff. Over the years,

this institution has provided training for physicians, teachers, professors, and editors in this special branch of medicine. Approximately 10 years ago it became apparent to the medical staff and to its Board of Directors that the Wills Hospital might extend its contribution to society by inaugurating a separate Research Department.

It is well known that medical research improves the physician's judgment of medical literature, sensitizes him to inadequacy of evidence, increases his awareness of exaggerated claims, and tempers his acceptance of enthusiastic predictions. Research reveals the difficulties of uncovering new facts. It insists that the investigator pay attention to what may seem to be unimportant details. Medical research demands team work, for rarely is modern research carried on by the lone investigator. The individual who is properly trained in research develops a respect for persistent routine. In institutions where active clinical and basic research is under way, the patient usually gets the most detailed attention.

The Research Department of the Wills Eye Hospital was informally initiated in 1948 under the direction of Irving H. Leopold, M.D. The first laboratory occupied a very small space in the basement of the hospital (figs. 1 and 2).

A small building was acquired in 1952 and refurnished for research pursuits (figs. 3 and 4). The department was tentative and uncertain. The confidence expressed in it at the original dedication by the late Justice of the Supreme Court, Owen J. Roberts, was not completely shared by those concerned with its future. Since that time, however, the research department's activities have increased, its personnel has more than doubled, and its interests have spread in many directions. The laboratory has consolidated its position in the field of ophthalmologic research.

Fig. 2 (Leopold). The first laboratory space in the basement of the Wills Eye Hospital.

Fig. 1 (Leopold). The first laboratory space in the basement of the Wills Eye Hospital.

Fig. 3 (Leopold. Original Wills Eye Hospital research building before renovation.

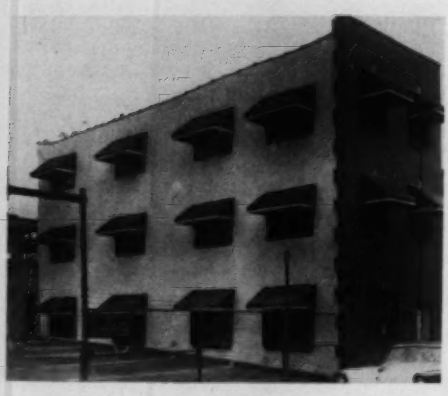


Fig. 4 (Leopold). Original Wills Eye Hospital research building after renovation.

teaching, and training in the United States.

As the need for additional space became acute, a contribution of the Ford Foundation, other gifts, and matching National Institute of Health funds made possible the construction of a new building for the research department. These new quarters were dedicated on September 20, 1959. Following is the program of the dedication ceremonies which were held at the Wills Eye Hospital at 16th and Spring Garden Streets, Philadelphia:

DEDICATION CEREMONIES

Opening Remarks

Mr. J. Griffith Boardman, Chairman, Committee on Research; Board of Directors of City Trusts

Invocation

Rev. John C. McGlade, C.S.Sp., Director, St. Joseph's House for Boys

Welcome to Wills Eye Hospital

Mr. Samuel H. Daroff, President, Board of Directors of City Trusts

Greetings from the Medical Staff

Wilfred E. Fry, M.D., President, Board of Attending Surgeons, Wills Eye Hospital

Comment

Mr. John A. Diemand, Former President, Board of Directors of City Trusts

Remarks

Edwin B. Dunphy, M.D., Henry Willard Williams Professor of Ophthalmology, Harvard Medical School and Chief of Ophthalmology, Massachusetts Eye and Ear Infirmary

A. E. Maumenee, M.D., William Holland Wilmer Professor of Ophthalmology and Director of Department of Ophthalmology, Johns Hopkins University School of Medicine

Irving H. Leopold, M.D., Director of Research, Wills Eye Hospital and Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania

Address

His Excellency—David L. Lawrence, Governor, Commonwealth of Pennsylvania

Benediction

Rev. Jerry E. Carpenter, Director, Institutional Chaplaincy, Episcopal Community Services

Tour of New Research Laboratory

Dr. Wilfred Fry pointed out that there have been three important steps in the career of the hospital. The first occurred when James Wills provided the funds to start the institution; the second, when the present hospital was built and dedicated in 1932; and the third was the advent of the research laboratory.

Both the president of the Board of Directors, Mr. Samuel Daroff, and Mr. J. Griffith Boardman, chairman of the Committee on Research, affirmed the support and the enthusiasm of the Board of Directors of Wills Eye Hospital for furthering research in the interests of providing the best possible care not only to those who attend this institution but to others, throughout the world, who are afflicted with ocular disease.

The Honorable Mr. David Lawrence, the Governor of Pennsylvania, expressed the thanks of the state for the contributions of the Wills Hospital to the welfare of its residents and all those who have entered its doors, and expressed his confidence in the hospital's future capacity for service.

Mr. John A. Diemand, head of the Insurance Company of North America and former president of the Board of Directors of Wills Eye Hospital, emphasized the necessity of adequate recompense for the research worker in the pursuit of his investigations.

Included in the roster of speakers at the dedication ceremonies were Dr. Edwin Dunphy of Harvard Medical School and Dr. Edward Maumenee of The Johns Hopkins

School of Medicine. Following are excerpts of their respective remarks:

DR. DUNPHY: All of us in ophthalmology and related branches of medicine are aware of the illustrious history of the Wills Eye Hospital. In 1931, Dr. William Campbell Posey and Dr. Samuel Horton Brown published a book entitled *The Wills Hospital of Philadelphia* to commemorate the 100th anniversary of its founding. I have recently re-read this book and would like to quote one paragraph which I think is a great tribute to the wisdom and foresight of the authors. Here is what they said:

"Good clinical work has always been done in the Wills Hospital and thousands of patients have obtained untold benefit from the treatment they have received but the eye hospital of the future must do more than treat diseases of the eye—it should be an institution to determine the nature of such morbid processes as well, and to look to their prevention."

How right they were! The Wilmer Institute had been established at Johns Hopkins in 1925 and the Howe Laboratory of Ophthalmology at Harvard in 1928. Then came the Oscar Johnson Institute at Washington University in 1931, the Institute of Ophthalmology at Columbia in 1933 and, more recently, the Proctor Laboratories at the University of California in 1954. Thus, the past 30 years has been the age of research in American ophthalmology and with it has come the realization that there must be integration between clinical ophthalmology and basic science if the patient is going to receive the maximum medical care. The Wills Eye Hospital, with its unsurpassed clinical facilities, is an ideal place for such integration to take place.

You now have created the atmosphere to orient young men toward research and to stimulate them to find the cause of many ocular diseases, the etiology of which is still unknown. All your residents will not follow this path of inquiry any more than mine will up in Boston. Only certain ones are fitted for a career of investigation. But you cannot fail with your present set-up to ignite the spark that may be lying dormant in some young man and launch him into the world of discovery.

DR. MAUMENEE: Today the problem is somewhat different, for the clinician and the laboratory investigator no longer has a relatively virgin field in which to work. There are few physicians who would deny that the opportunities for major advances in surgical technique or clinical classification of disease are less than they were in the past. Also it is less likely that the laboratory worker equipped with running water, a few pieces of string, some sticks, a microscope, and an idea will contribute as frequently to our progress. This does not mean, however, that there are no problems to be solved for, while we can diagnose diabetic retinopathy, senile macular degeneration, and ocular tumors, we are almost as ignorant of their cause as our predecessors. We can remove cataracts, reattach retinas, transplant corneas, and lower intraocular pressure in glaucoma, but we know little of the processes which create the disease we are treating.

To solve these problems we must enlist the aid of the biochemist, the modern physiologist, the physicist, the biostatician, the immunologist, and the microbiologist. Our laboratories must be equipped with highly complicated equipment, electron microscopes, and facilities for handling radioactive isotopes and tissue cultures.

One might ask—if future progress in ophthalmology is to be accomplished by such highly specialized workers with such complicated equipment, should not these workers be delegated to the basic science departments in medical schools rather than the clinical departments of ophthalmology? There are several answers to this question:

First, the basic scientist needs instruction from the clinician in regard to disease processes.

Second, the results of laboratory investigations have to be applied to the patient before their ultimate value can be determined.

Third, the clinical practice of medicine is always better when the physician is aware of the progress that is being made in the experimental laboratory.

Finally and probably most important of all, every resident in ophthalmology should be exposed to laboratory experimental work for it not only teaches him to make a critical evaluation of his own clinical work and the published work of others but also one never knows which resident may be stimulated to make an outstanding investigator.

Dr. Leopold, the director of the laboratories since their inception, thanked all the friends of the institution and its staff for their considerable support.

The new laboratory (fig. 5) consists of two floors providing approximately 5,000 square feet of air-conditioned space. There are laboratories devoted essentially to pharmacology, biochemistry, histopathology, microbiology, and studies with radioactive isotopes. The older research building, dedicated

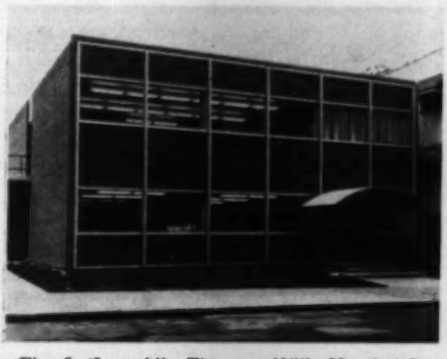


Fig. 5 (Leopold). The new Wills Hospital Research Laboratory which was dedicated on September 20, 1959.

in 1952, will continue to be used for active investigations and will continue to house experimental animals.

Although dedicated research workers can strive to their full human capacities with the most meager equipment, this new building, with its many modern facilities, will unquestionably speed the results of the efforts of those at Wills. The entire staff of the Wills Eye Hospital Research Laboratory is looking forward to new opportunities for significant service to the community, to the country, and to the world.

Irving H. Leopold.

OBITUARY

EDMOND VELTER
(1884-1959)

Prof. Edmond Velter, chief ophthalmic surgeon at the Hotel Dieu de Paris, ex member of the International Council of Ophthalmology, died at his country house near Versailles on July 2, 1959. He was well known in the United States and in Canada which he visited several times on missions of the Faculté de Paris.

Edmond Velter was born in Paris, the son of an engineer. He had a scientific education and after interning, he became an ophthalmic surgeon of the Paris Hospitals, agrégé de la Faculté and a professor when Prof. Terrien died in 1939.

During his successful career he wrote many books and papers. The first one was on "Optic Neuritis in Disseminated Sclerosis" (these of Paris, 1912). It is an exhausting review of that difficult question which, after 50 years, is still up to date. During the first world war, Velter was a military ophthalmic surgeon and, after 1918, he published a book on war eye injuries. A very skillful surgeon, he was a pioneer in neurosurgery. Ophthalmoneurology was always his specialty. He wrote papers and gave reports on pupillary reflexes, oculomotor palsies and wrote important chapters of the *Traité d'Ophtalmologie* (Masson, 1939). His main works were the *Atlas of Biomicroscopy of the Lens* (with Duverger) and a *Traité de chirurgie oculaire* (with Duverger and Brégeat).

Velter thought that ophthalmology should be closely connected with general pathology and with Tournay he was founder of the Otoneuro-ophthalmological Society.

Velter was the father of four children, one an ophthalmologist. Not only was he a learned scholar, a good teacher, and a skillful surgeon, he was a man of a great spirit and courage. During the years of German occupation in France he became a member of resistance organizations and, in 1944, he was sent to prison at Versailles. He would probably have been shot had not his warden, a patient he had cured, given him the means of escape.

His pupils, friends, and many ophthalmologists all over the world will remember Velter's lofty stature and handsome head, eloquent speech, and his clear useful books will remain classic for a long time.

René Onfray.

CORRESPONDENCE

ADMINISTRATION OF UREA FOR REDUCTION OF INTRACRANIAL AND INTRAOCULAR PRESSURE

Editor,
American Journal of Ophthalmology:

Because of the current popularity of administration of urea for reduction of intracranial pressure by neurosurgeons and for reduction of intraocular pressure by ophthalmic surgeons, as presented by John M. McLean, M.D., and his associates, in the September, 1959, *Archives of Ophthalmology*, the following previously unpublished data may be of interest.

The data were obtained in 1936 and permission for publication at this time has been granted by Frank Fremont-Smith, M.D., and Dorothy Sloan McClintock, A.B., who would have been co-authors with me of an article from the Department of Neuropathology of the Harvard Medical School, Neu-

rological Unit of the Boston City Hospital and Psychiatric Unit of the Massachusetts General Hospital, if all three investigators had not left Boston before preparing the paper for publication. After a recent discussion with Dr. McLean, I felt that it might still be worthwhile to call attention to these data, even after the lapse of 23 years.

In a study of the equilibrium between blood serum and cerebrospinal fluid, the relative distribution of urea between these fluids is important because urea is one of the most soluble and most readily diffusible substances normally present in the blood. Because elimination of urea from the blood stream is rapid in a person with normal kidney function, repeated doses of urea were given, in some of the experiments, to keep the blood urea value high for a period long enough to allow the cerebrospinal fluid to become equilibrated with it in respect to this constituent, by formation of fluid from blood of higher urea content or by diffusion of urea into fluid previously formed. The purpose of this series of experiments was to reach more definite conclusions as to the time factor involved in the relationship between blood and spinal fluid urea content after ingestion of urea in order to explain contradictory reports as to the diffusibility of urea and the relative concentrations of it in spinal fluid and blood.

Had this data been published and discussed, with particular attention called to the cerebrospinal fluid pressure which was, in some cases, "too low to read in the manometer," and to the complaint of a "lumbar puncture type headache" that sometimes followed ingestion of urea, some neurosurgeon might have made practical use of the findings years ago. The interest of the investigators was limited to factors influencing diffusion of urea, factors which would be related to the formation and absorption of aqueous humor as well as cerebrospinal fluid.

The technique of lumbar puncture and methods of examination of the serum and spinal fluid are described in *The Cerebrospinal Fluid* by H. Houston Merritt, M.D., and Frank Fremont-Smith, M.D., Saunders (Philadelphia, 1937). The methods are still acceptable. I am presenting this data (series I, II, and III) with no comment other than a suggestion that ophthalmic surgeons, when using urea, especially intravenously, consider

SERIES I

DIAGNOSES: (1) Mastoiditis, no central nervous system involvement; (2) general paresis; (3) general arteriosclerosis, right hemiplegia; (4) old central nervous system lues; (5) polyneuritis. *A*. After overnight fast. Patient then given 60 gm. urea in tomato juice, then 30 gm. in four hours and another 30 gm. four hours later. *B*. After overnight fast; 24 hours after first dose of urea was given.

Case No.	Urea Nitrogen (mg./100 cc.)		Cerebrospinal Fluid		
	Serum	C.SP.FL.	Initial Pressure (mm. c.sp.fl.)	Cells (per cu. mm.)	Total Protein (mg./100 cc.)
1. *A*.	8	8	130	1 wbc	38
B.	35	33	90	4 wbc	47
2. *A*.	21	21	150	165 rbc; 4 wbc	154
B.	50	49	150	1,300 rbc; 27 wbc	170
3. *A*.	19	18	170	9 rbc; 0 wbc	48
B.	43	47	160	14 rbc; 657 wbc	74
4. *A*.	10	9	cistern puncture	1 wbc	18
B.	23	25	cistern puncture	2 wbc	21
5. *A*.	17	15	170	2 wbc	196
B.	27	35	190	128 rbc; 1 wbc	160

In these five cases, urea values in blood serum and cerebrospinal fluid are markedly increased 24 hours after urea ingestion. The data indicate that ingestion of urea does not give sustained lowering of intracranial pressure but that normal pressure levels are re-established when serum and spinal fluid urea values have reached equilibrium at the higher level.

SERIES II

DIAGNOSES: (6) Psychoneurosis; (7) softening of brain after cerebral hemorrhage; (8) aseptic lymphocytic meningitis. *A*. After overnight fast. Patient then given 60 gm. urea in tomato juice, then 30 gm. four hours later. *B*. 9.5, 9.0 and 8.25 hours respectively after first urea by mouth. *C*. In Case 8, third lumbar puncture following morning.

Case No.	Time	Urea Nitrogen (mg./100 cc.)		Cerebrospinal Fluid		
		Serum	C.SP.FL.	Initial Pressure (mm. c.sp.fl.)	Cells (per cu. mm.)	Total Protein (mg./100 cc.)
6. *A*.		13	11	150	200 rbc	53
B.		74	27	0	—	—
7. *A*.	9:30 A.M.	13	13	220	4 wbc	276
	Urea	—	—			
	11:00 A.M.	66	—			
	1:30 P.M.	58	—			
	Urea	—	—			
	4:00 P.M.	83	—			
B.	6:30 P.M.	74	64	0	110 rbc; 190 wbc	408
8. *A*.	9:00 A.M.	15	13	160	32 wbc	34
	Urea	—	—			
	11:00 A.M.	44	—			
	2:15 P.M.	52	—			
	Urea	—	—			
B.	5:30 P.M.	59	36	0		48
C.	9:00 A.M.	22	31	0	1,500 rbc; 110 wbc	—

In these three cases, urea values were considerably higher in serum than in cerebrospinal fluid at the time of the second lumbar puncture and cerebrospinal fluid pressure was too low to read in the manometer. This data is evidence of the dramatic lowering of intracranial pressure by ingestion of 90 gm. of urea.

the extreme precipitous reduction in intracranial pressure coincident with the sudden reduction of intraocular pressure and appreciate situations in which this sudden drop in pressure might be contraindicated.

These 10 experiments demonstrate diffusibility of the urea molecule, as expected because of its relatively small size, and effectiveness of urea in reducing spinal fluid pressure by the osmotic effect of the urea molecule and, in Cases 5 and 10, with spinal fluid urea higher than the coincident serum urea, a reversal of this effect. These facts indicate that urea is useful for acute lowering of intraocular and intracranial pressure but not for a sustained effect.

(Signed) Mary D. Irvine, M.A.

(Mrs. S. Rodman Irvine.)

SERIES III

DIAGNOSES: (9) Undetermined; (10) low back strain. *A*. After overnight fast. *B*. Five hours after urea by mouth; 30 gm. in Case 9 and 60 gm. in Case 10.

Case No.	Urea Nitrogen (mg./100 cc.)		Cerebrospinal Fluid		
	Serum	C.SP.FL.	Initial Pressure (mm. c.sp.fl.)	Cells (per cu. mm.)	Total Protein (mg./100 cc.)
9. *A*.	14	13	120	1 wbc	37
B.	36	17	0	2 wbc	52
10. *A*.	24	22	120	0	34
B.	22	49	140	300 rbc; 1 wbc	37

In these two short experiments we see: In Case 9—urea concentration, after ingestion of urea, higher in serum than in spinal fluid and cerebrospinal fluid pressure reduced to a value too low to read because formation of new spinal fluid is not keeping pace with the increased absorption caused by the hypertonicity of the blood. In Case 10—blood urea back to normal level but spinal fluid urea lagging in its return to normal, with the higher concentration of urea in the spinal fluid causing reversal of the osmotic effect and spinal fluid pressure, as in Case 5, slightly higher than at the original lumbar puncture.

BOOK REVIEWS

NEURO-OPHTALMOLOGIE. By L. Guillaumat, P. V. Morax, and G. Offret. Paris, Masson et Cie, 1959. 1388 pages in two volumes, 464 figures, 11 color plates, references, index. Price: Unbound, 19,000 francs; bound, 21,500 francs.

Guillaumat is ophthalmologist to the National Center of Ophthalmology of Quinze-Vingts, Morax is ophthalmologist to the Hospital of Paris, and Offret is professor "agrégé" of the Faculty of Medicine in Paris and ophthalmologist to the hospitals. Each is an eminent authority, widely known for his contributions. Together, they have brought out a work that is definitive and formidable. It is a great achievement and those of us who cannot read French are great losers thereby.

The first volume (652 pages) is titled "Neuro-ophthalmologic seminology." The second volume (693 pages) is titled "Neuro-ocular diseases from diverse affections of the nervous system." If there is anything missing from this complete coverage of the subject of neuro-ophthalmology which incidentally had its birth in France with the works of Parinaud and Babinski, I have been unable to detect it.

The text is lively and characteristically clear, as the French authors seem to write. The illustrations are excellent and the colored plates exceptionally good.

Although we have our brilliant *Clinical Neuro-Ophthalmology*, by Frank Walsh to lean on, it would be good if these two fine French volumes were to be translated into English.

Derrick Vail.

VISUAL HANDICAPS (VISUEEL GEHANDICAPTEN). Symposium by 32 contributors. Grave, Holland. St. Henry's Institute, 1959. 332 pages, 12 photographs. Price: Not listed.

This commemorative volume is a tribute to the centennial of St. Henry's Institute at Grave, Holland. Originally founded for the education of blind boys, its program has extended to the semisighted and 138 pupils are now enrolled. The institute was established, maintained and enlarged by private contributions solely. It pioneered in braille instruction and has developed many special educational appliances, including the "arithmetic box" which has been adopted for blind students in Grand Rapids, Michigan. The contributors to this volume cover the problems of the visually handicapped from every phase. Besides the 26 Dutch papers, there are two each in French (P. Bailliart and P. Henri), German (C. Strehl and A. Fischer) and English (J. F. Clunk and J. E. Lebensohn). The Dutch writings include essays by Professors Kijn, Strasser, Van den Heuvel, van Houte, Weve and Zeeman. Schappert-Kimmijser presents in summary his elaborate study on the causes of blindness in Holland.

James E. Lebensohn.

CARCINOGENESIS: MECHANISMS OF ACTION. Edited by G. E. W. Wolstenholme and M. O'Connor. Ciba Foundation Symposium. Boston, Little, Brown and Company, 1959. 336 pages, 48 illustrations, index. Price: $9.50.

Carcinogenesis in the eye, as elsewhere, remains a deep mystery. This symposium presents the various theories put forth and the reader will search in vain for a clue as to the etiology of the familiar ocular cancers. However, there is much of value in this volume. A full discussion of tumor production by the subcutaneous implantation of plastic films gives rise to a slight uneasiness when one considers the abandon with which plastic materials are being implanted into and onto the eye. The relationship of cancer to viruses is also explored and it is concluded that with the exception of leukemia in children "no type of malignancy in man has yet provided any significant evidence of being mediated by virus-like agents."

If one generality can be made from a pe-

rusal of this book, it is that it is extremely unlikely that one biochemical lesion can explain all malignant tumors. Recommended to ocular pathologists and biochemists.

David Shoch.

THE SURGEON AND THE CHILD. By Willis J. Potts, M.D., surgeon-in-chief, Children's Memorial Hospital, professor of pediatric surgery, Northwestern University Medical School, Chicago. Philadelphia, W. B. Saunders Company, 1959. 225 pages. Price: $7.50.

This text by an outstanding pediatric surgeon contains no reference to ophthalmic surgery in the child but is concerned particularly with congenital and developmental anomalies of the chest and abdomen. Its only direct interest to the ophthalmologist lies in the discussion of general anesthetics in children and the psychologic and philosophic considerations of the handling of infants during examination and in the hospital.

William A. Mann.

A SYNOPSIS OF ANESTHESIA. By J. Alfred Lee, M.R.C.S. Baltimore, Williams & Wilkins, 1959. Price: $6.50.

Few fields of medicine are changing and improving as rapidly as the practice of anesthesia. The fourth edition of *A Synopsis of Anesthesia* is a complete revision. Many new illustrations and two new chapters, one on the phenothiazine derivatives and one on induced hypothermia, are added. There is also a new section on halothane (Fluothane).

The format of the book is in a modified outline form which begins with the historical background of anesthesia and ends with the postoperative recovery room. It is a singularly excellent book for the beginner. It allows him to learn principles, anatomy, physiology, pharmacology, and so forth, of anesthesia, in a clear and uncluttered form. With this background he may then follow through with more specific types of literature.

As a whole the book lacks international scope in its bibliography. In reviewing it, one finds that most of the references and all of the illustrations come from the British literature.

The new revision is a book that should be in the library of every anesthesia department. It should serve as a stimulus to the student for wider reading.

Lucille Watt.

CURRENT VIRUS RESEARCH. British Medical Bulletin, Volume 15, No. 3, September, 1959. Medical Department, The British Council, 65 Davies Street, London, W.1. Price: $3.25.

This symposium on current virus research was prepared under the chairmanship of C. H. Andrewes by 18 British virologists. It covers new techniques and methods in use in virus research, discoveries of new viruses, and observations on the genetic, biochemical, epidemiologic, and epizoologic aspects of virology. A chapter of special interest was contributed by A. Isaacs and D. C. Burke on viral interference, a phenomenon mediated by a substance, probably a protein, called "interferon" by the authors.

Three chapters have special interest for ophthalmologists. The first, contributed by A. W. Downie, considers zoster and chickenpox and summarizes recent evidence indicating the identity of the two causal viruses. He accepts the currently held belief that zoster is a second and more localized tissue invasion with varicella virus. The second chapter of interest to ophthalmologists is the one on trachoma and inclusion conjunctivitis by L. H. Collier in which he shows that trachoma virus can now be cultivated in series and in quantity, and that a similar agent can be cultivated from inclusion conjunctivitis. Both these agents possess the complement-fixing group antigen of the psittacosis-lymphogranuloma group of viruses. The way is now open for a much more complete understanding of these two diseases and for possible advances in therapy and prophylaxis. The third chapter in this category of

interest is the one on adenoviruses by H. G. Pereira in which he summarizes present knowledge of this interesting group, more than 23 serologic types of which had been described by 1958. Type 8 is now established as the cause of epidemic keratoconjunctivitis, and type 3 as the usual cause of pharyngo-conjunctival fever. Sporadic cases of acute follicular conjunctivitis have been caused by other adenovirus types. The group is an important cause of respiratory illness.

The symposium concludes with a chapter by F. Fenner on myxomatosis, a mild disease of South American rabbits but a highly fatal disease of European and Australian rabbits. The volume can be highly recommended to all those with an interest in the rapidly advancing field of virology.

Phillips Thygeson.

KERATOPLASTY. By Wiktor Arkin. Warsaw, Government Medical Publishing Office, 1956, XII. Color plates, 270 pages, 132 illustrations, bibliography. Price: 42:60 Zloty.

Prof. Arkin presents Polish ophthalmologic literature with the first monograph on corneal transplants. It starts with a short chapter on history and classifications of transplants followed by a detailed description of instruments used by the author and others in this type of operation. Partial and subtotal transplants are treated separately. Detailed technique is given, starting with the preparation of the patient and going through various methods of preparing the transplant, the patient's cornea and suturing of the transplant.

Postoperative care is given due attention and possible complications are described together with the steps which should be taken to avoid them or to treat them. The problem of clouding of the transplant is given special attention. Indications and contraindications for the operation are discussed extensively. Total corneal transplant is described in a special chapter where techniques of Szymanowski, Filatov, and Castroviejo are especially singled out. The author considers this operation to be the most difficult in corneal surgery.

The methods of lamellar transplants are presented in the same thorough way, giving details of techniques of numerous authorities. Again postoperative care and possible complications are described. Surprisingly, indications for this operation are given at the end of this part of the book. The author discusses in a separate chapter corneal transplants for treatment of the cornea as a step for further corneal surgery. Reconstruction and cosmetic keretoplasty are also discussed.

The last third of the book treats the problem of the donor material. Microscopic and bichemical studies are described. The whole material is presented systematically and clearly. The language is simple and it is regrettable that because of the language barrier this monograph will be known to a limited number of ophthalmologists.

Sylvan Brandon.

HANDBOOK OF PHYSIOLOGY. SECTION I: NEUROPHYSIOLOGY, VOLUME I. Edited by John Field, H. W. Magoun, Victor E. Hall. Baltimore, Waverly Press, Inc., 1959. 779 pages; dimensions: 11 by 9 by 1.5 inches, weight five pounds. Price: $22.00

This is the first volume of a series entitled *Handbook of Physiology* to be published by the American Physiological Society. Additional volumes to include the entire field of functional biology are planned for completion in approximately 10 years. It is called a handbook, which hardly suits its five pounds and considerable dimensions, but its distinguished editors have made every ounce worth while.

This volume, the first of three devoted to neurophysiology, is divided into four major sections preceded by a captivating historical review by Mary Brazier. Each section is introduced by a veteran in that special domain —Eccles, Fessard, Adrain, Hartline—and the individual chapters (a total of 31) are

contributed by men outstanding in their particular subject. The three first sections deal with (a) Neuron physiology, (b) Brain potentials and rhythms, and (c) Sensory mechanisms. At first glance these might seem of remote interest to the ophthalmologist but the eye is not only a sense organ, it is also a displaced part of the brain and it contains millions of neurons.

The fourth section called "Vision" will be of most interest to the ophthalmologist. This section is introduced by Keffer Hartline of the Rockefeller Institute of Medical Research, well known indeed to everybody interested in visual physiology. The chapter by Lorus and Margery Milne, both biologists at the University of New Hampshire, is concerned entirely with photosensitivity in invertebrates. After describing the basic concepts of photosensitivity in general, the authors draw a most interesting picture of different types of responses to light stimuli in organisms lacking eyesight and the adaptability of vision according to the needs of the organism.

Glenn Fry, The Ohio State University School of Optometry, in the next chapter gives an account of the image-forming mechanism of the eye. The content is the usual one encountered in ophthalmologic text books.

In the chapter by George Wald, Harvard, the reader is familiarized with the photoreceptor processes in the eye. The author's writing is, as usual, crystal clear, which makes the text fascinating and easily understood by the nonbiochemist. The first part of the chapter describes the biochemistry of the visual pigments which is now quite well known—to a large extent due to work of the author and his collaborators. It also deals with the almost completely unknown mechanism by which chemical events are translated into electric activitiy.

In the latter half of the chapter the author discusses physiologic correlations, pointing out that many of the basic features of vision (Purkinje shift, light-adaptation and dark-adaptation, and so forth) directly reflect the properties of retinal molecules. A discussion on vitamin-A deficiency and nightblindness concludes the chapter.

Ragnar Granit, Sweden, has written the chapter on neural activity of the retina. He combines a life-long laboratory experience of his own with an incredibly large amount of knowledge of the field to summarize present knowledge concerning both the electric mass response of the eye (electroretinogram) and electric activity of single cells in the retina. Granit concludes with some remarks about the use of electroretinograms in clinical ophthalmology. Those readers who are only looking for some orientation in the vast field of neurophysiology of the eye will find it here. Those who seek a thorough understanding of the subject will find the chapter a good start as they are led by the expert through the jungle of neurophysiologic literature.

The two last chapters are both concerned with central mechanisms. One of these, by Howard Bartley of the Michigan State University Department of Psychology, deals only with vision. He first gives a definition of vision, then proceeds to a description of (a) phenomena of vision, and (b) neurophysiologic findings pertaining to the optic pathways above the retinal level. He concludes by correlating these two sets of data. The author's approach is largely that of the psychologist and the reasoning not always easy to follow.

The final chapter written by Robert Livingstone, National Institute of Neurological Diseases and Blindness, Bethesda, gives a concise and informative presentation of the central control of receptors and sensory transmission systems in general, including the latest findings concerning centrifugal control of the retina.

This first volume of the *Handbook of Physiology* admirably fulfills a long-standing need for a summary of current knowledge in neurophysiology.

Christine Enroth.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Gilkes, M. **Trachoma in Jordan and the Gambia.** Tr. Ophth. Soc. U. Kingdom **78**: 227-243, 1958.

A small group in 1955 attempted isolation of the trachoma virus in Jordan and the development of a vaccine. They began activities in Jerusalem with laboratory facilities provided by the Ophthalmic Hospital of the Order of St. John. Arab patients attending clinics in refugee camps and in villages were examined. Conjunctival scrapings were taken from patients who fulfilled the criteria for diagnosis of trachoma and conjunctival cultures were taken in all cases.

The presence of inclusions of Halberstaedter and von Prowazek were regarded as the only satisfactory positive evidence of potential infectivity. Six cases were found after two months work; 5.5 percent of 5,000 patients examined and 18 percent in a special series of 70 cases had the inclusions. Approximately 80 percent of all patients over 25 years of age showed the clinical sign of trachoma in Stage IV. (8 figures)

Beulah Cushman.

de Vincentiis, M. **Effect of xanthopterin on the experimental wounds of the cornea.** Acta ophth. **37**:290-293, 1959.

Xanthopterin ointment (0.1 percent) accelerated the healing of experimental corneal abrasions in rabbit eyes. (1 figure, 1 table, 6 references) John J. Stern.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alajmo, Arnaldo. **Activity of the enzyme rodanese in the retina and in the lens.** Gior. ital. oftal. **10**:284-289, July-Aug., 1957.

The lens and the retina both show a weak activity of the enzyme rodanese, probably because of the marked aerobic glycolysis of these tissues. Because of the high content of vitamin C in the lens one cannot correlate the activity of rodanese with vitamin C content of the tissue. (2 tables, 10 references) V. Tabone.

Berggren, L. **Further observations on the appearance of fluorescein in the rabbit eye after intravenous injection.** Acta ophth. **37**:215-218, 1959.

Sections from rabbit eyes, frozen at different intervals after an intravenous fluorescein injection and examined under ultraviolet light show that a "cloud" in the pupil can originate either in the anterior or posterior chamber. As long as it is not possible to differentiate between flow from the posterior chamber and diffusion into the anterior chamber, a large source of error is introduced into the determination of the time of appearance. (1 figure, 3 references) John J. Stern.

Brolin, S. E. and Hammar, H. **The fluorescence of the eye lens in rats after local Roentgen irradiation. A spectrophotometric investigation.** Acta ophth. **37**:266-273, 1959.

Cataracts were induced in rats' eyes by X-ray irradiation. At the incipient stage the fluorescence of the lens was increased by 17 percent. At the mature stage it was decreased by 31 percent. The spectral distribution was only slightly changed. The increase may be explained by initial damage to the ciliary body which would allow fluorescent compounds to pass the secretory epithelium; the decrease in mature cataracts might be due to dilution of the same compounds in the lens by fluid absorption. (3 figures, 22 references)
John J. Stern.

Christensen, H. **Visually observed traces of high frequency eye vibration.** Acta ophth. **37**:227-233, 1959.

The physiologic rapid vibration of the eye during fixation is measured by observing a figure with narrow black-and-white stripes. Narrow contrast stripes approximately 4 μ wide will appear on their horizontal border; they correspond to film records made of the eye vibration. Both contrast stripes are memories during the eye movement. (2 figures, 10 references)
John J. Stearn.

Forlani, D. and Frasca, G. **A study of the oculo-ocular reflex in rabbits.** Boll. d'ocul. **37**:775-793, Oct., 1958.

The authors found that the systemic administration of chloropromazine did not inhibit the consensual pupillary light reaction. They did find, however, that it was possible to block this consensual light reaction by retrobulbar administration of this drug to the eye in which the consensual light reaction is to be observed. Retrobulbar administration of this drug behind the eye in which the direct pupillary reaction is to be observed did not block the consensual light reaction. They also found that contrary to what occurs in man, the retrobulbar injection of chloropromazine in rabbits produced an elevation of the intraocular pressure in both the ipsolateral and contralateral side. (8 figures, 7 references)
Joseph E. Alfano.

Heaton, J. M. **Vitamin B_{12} and herpes zoster ophthalmicus.** Brit. J. Ophth. **43**: 438-439, July, 1959.

Vitamin B_{12} was given in large doses to 16 patients with herpes zoster about the eyes in a controlled experiment. The drug had no effect on the course of the disease and it was shown that not only was there no deficiency of the vitamin in these patients but that the extra drug given was promptly excreted. (5 references)
Morris Kaplan.

Kleifeld, O. and Neumann, H. G. **The oxygen content of the human aqueous.** Klin. Monatsbl. f. Augenh. **135**:224-226, 1959.

The oxygen content of the aqueous was measured in the eye of 12 patients. The specimen was obtained by anterior chamber puncture. The mean value for 12 eyes was 2.1 gamma/ml, the variations ranged from 1.5 to 2.7 gamma/ml. (1 table, 4 references) Gunter K. von Noorden.

Lembeck, F. and Hofmann, H. **Further experimental investigation of enzymatic zonulolysis.** Klin. Monatsbl. f. Augenh. **135**:232-240, 1959.

The authors investigated the action of alpha-chymotrypsin, trypsin, and proteinase of bacillus subtilis N′ on rabbit cornea which had been deliberately punctured from the endothelial side. Corneal opacities of various degree were observed depending on the concentration of the enzyme injected into the anterior chamber. The damaging effect of trypsin equalled that of alpha-chymotrypsin only when the former was used in a concentration four times as high. The zonulolytic effect of trypsin, however, is three times as high as that of alpha-chymotrypsin.

In another series of experiments the authors found the proteinase of bacillus subtilis to possess zonulolytic properties. This enzyme, however, if used in concentrations as low as 1,000 units/ml led to severe damage of the previously traumatized rabbit cornea. Lysozyme and hyaluronidase were ineffective in producing zonulolysis. Enzymatic zonulolysis occurs only when the zonular fibers are under tension. This should be considered in the technique of extraction. The action of the enzyme is thus enhanced when traction sutures through the four rectus muscles are used. (4 figures, 1 table, 5 references)

Gunter K. von Noorden.

Pines, M. **Retinal capillary circulation.** Tr. Ophth. Soc. U. Kingdom **78**:275-277, 1958.

After his experimental work and a review of the literature the author states that the retinal capillaries remain permanently open, and that retinal metabolism is the highest in the body but the retinal capillary circulation is not fully understood.

Beulah Cushman.

Salvi, G. and Lepri, G. **Comparative studies of the mydriatic and cycloplegic effects of N-ethyl-N-(gamma picolil-) amide of tropic acid, homatropine, labatropine, and cyclogyl.** Arch. di ottal. **63**: 239-252, May-June, 1959.

Mydriatum (Roche) has a greater and briefer effect as a cycloplegic and as a mydriatic than does cyclogyl. (3 figures, 8 references)

Paul W. Miles.

Sampaolesi, R. and Blumenkrantz, N. **Pseudocrystallization of biologic fluids, with special reference to the aqueous humor.** Arch. oftal. Buenos Aires **33**:173-177, Aug., 1959.

This is a study of the microscopic appearance of dried drops of aqueous humor, vitreous and subretinal fluid. The pseudocrystallization of sodium chloride, which, in the case of the aqueous, would be due to the presence of hyaluronic acid, seems to follow different patterns in sound and in diversely diseased eyes. (7 figures, 16 references)

A. Urrets-Zavalía, Jr.

Sundmark, E. **The contact glass in human electroretinography.** Acta ophth. Suppl. 52, 1959.

This monograph is based on five papers published previously and abstracted in these pages. The main results of the author's experiments can be summarized as follows: 1. The potential of the ERG is maximal and constant on recordings from any point of the cornea but falls rapidly at the limbus and posteriorly. 2. The potential drop between posterior pole and the reference electrode on the forehead is 35 percent; between the vitreous and the border between the corneal and scleral parts of the contact glass it is 25 percent; between vitreous and posterior pole about 33 percent. 3. ERG recording with a contact glass having a scleral part as electrode, producing a thick precorneal fluid layer, is equivalent to strictly corneal re-

ording. 4. A contact glass suitable for human electroretinography must be made of inflexible, insulating, light-transmitting material; the scleral radius must be smaller than that of the eye; a thick precorneal fluid layer should be present; and the recording electrode must be placed in the corneal part, in contact with the fluid layer. (12 figures, 60 references)

John J. Stearn.

Sundmark, E. **Recording of the human electroretinogram with the contact glass. V. Studies of the potential distribution over the anterior surface of the eye and of the recording resistance.** Acta ophth. **37**: 219-226, 1959.

Recordings of the ERG with a wick electrode show that the b-potential is maximal and almost constant over the entire corneal surface and drops rapidly at the limbus and posteriorly. Recordings of the b-potential with a contact glass of ordinary size and with a corneal contact lens give identical results. Use of contact glasses of the same size but different material (perspex and rubber) results in a larger potential when inflexible material is used, even if an electrically insulating, water-repellent ointment is applied to the inner surface of a rubber contact "glass." (2 figures, 13 references) John J. Stearn.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Barraquer, Tomas. **Lenses as therapeutic agents, should be prescribed only by ophthalmologists.** Arch. Soc. oftal. hispano-am. **19**:309-310, April, 1959.

Barraquer deplored the fact that much of refraction is being done by optometrists, and emphasizes the effect of lenses on binocular vision and some ocular affections. After lens extraction for high myopia the increased sharpness of vision may cause a cerebral annoyance to patients not accustomed to such clarity of distant vision; in such cases it is necessary to prescribe only a partial correction and accustom the patient gradually to his full correction and markedly increased visual acuity. He reports the experience of two young students with high myopic astigmatism and lenses which gave them good distant visual acuity, but caused fatigue during near work. He found that the accommodation made necessary by the distant correction was accompanied by excessive convergence which caused the discomfort. A prescription for near work in which a plus-two diopter sphere was incorporated in the distant correction relieved the excessive convergence and asthenopia. Ray K. Daily.

Blomberg, L. H. and Wassén, A. **Preliminary report on the effect of alcohol on dark adaptation, determined by an objective method.** Acta ophth. **37**:274-278, 1959.

Intake of small doses of alcohol (20 ml. of 10 percent alcohol intravenously) did not influence the dark adaptation during the first 10 minutes. (1 figure, 4 references) John J. Stearn.

D'Esposito, M. **Clinical consideration of a system of increasing utilization in subnormal vision.** Arch. di ottal. **63**:211-226, May-June, 1959.

Of 103 patients with subnormal vision treated by magnifying devices 27 showed no improvement, 47 showed better vision, but did not accept the appliance, and 29 were improved and continued to use the device supplied. Most of the patients were given a telescopic lens, a few a microscopic lens, a loupe, or a strong reading addition. (1 table, 32 references)

Paul W. Miles.

Dreyer, V. **Visual contrast thresholds. III. The just perceptible and the just im-**

perceptible stimulus. Acta ophth. **37**:253-265, 1959.

A critical minimum visual angle is demonstrated for the just perceptible or just imperceptible positive or negative stimulus; below it a further reduction of the stimulus area leads to an increased demand for contrast. As long as a certain critical value of background luminance is exceeded, the area independence, demonstrated previously in the case of negative stimuli, is present only for the just imperceptible negative stimulus; the threshold luminances for the just perceptible stimulus show the same area dependence as those for positive stimuli, or as those for just imperceptible negative stimuli at lower background luminances. It is concluded that stimulation by a luminance which is greater than that of the background leads almost instantaneously to a drop in sensitivity of the retinal area stimulated. This drop is greater than the slower rise in sensitivity which follows a corresponding stimulation which is less than that of the background. (4 figures, 9 references) John J. Stern.

5

DIAGNOSIS AND THERAPY

Beiras Garcia, A. **Cinematographic orthoptics.** Arch. Soc. oftal. hispano-am. **19**:282-293, April, 1959.

The author describes an orthoptic procedure which combines synoptophore exercises with cinematographic exercises. The film has targets for each eye and the electromagnetic occluders synchronized with the film insure that each eye perceives its own targets. The cinepleoscope designed by the author can take the place of the occluding device. This procedure makes possible simultaneous treatment of a group of children, which may be of longer duration and more comfortable than exercises on the synoptophore. (4 figures) Ray K. Daily.

van Beuningen, E. G. A. **A new electric tonometer for tonometry, tonography, and measurement of ocular circulation.** Klin. Monatsbl. f. Augenh. **135**:184-188.

A new tonometer was developed and is now commercially available. The following measurements can be carried out with this instrument: tonometry, tonography, constant pressure tonography, isotonography, determination of pulse volume, basic flow, and retinal artery pressure. (5 figures, 4 references)

Gunter K. von Noorden.

Cambiaggi, A. **The clinical significance of the C-reactive protein in ophthalmology.** Boll. d'ocul. **37**:754-767, Oct., 1958.

The author found that the determination of the C-reactive protein was of no help in the diagnosis of uveitis and keratitis although he felt that it may have been of some help in evaluating the course of these diseases, particularly after fever therapy. (3 tables, 10 references)

Joseph E. Alfano.

Casanova, J. and Mir y Mir, L. **Improvement in the technique of orbital evisceration.** Arch. Soc. oftal. hispano-am. **19**: 249-260, April, 1959.

The author reports a case of a myxoma of the orbit, in which an exenteration was performed by Reese's technique saving the anterior layers of the lids and implanting the temporal muscle into the orbit. In addition the authors introduced a stent inlay covered with skin excised from the abdomen for the provision of a pouch for an artificial eye. The surgical technique is described in detail and the final results which appear cosmetically satisfactory are illustrated. (9 figures)

Ray K. Daily.

D'Esposito, M. **Another indication for a system of magnification: the treatment of amblyopia ex anopsia.** Arch. di ottal. **63**:233-238, May-June, 1959.

The author advises the use of magnifying lenses before an eye with amblyopia ex anopsia when the other eye is lost. Experience with such eyes has convinced him that a magnifying lens is a good treatment for amblyopia ex anopsia, even when the other eye is normal. (5 references) Paul W. Miles.

Garigali, F. and Bonaccorsi, A. **Association of hydrocortisone, neomycin and gramicidin in the treatment of inflammatory processes of the anterior segment of the eye.** Rassegna. ital. d'ottal., **28**:169-180, May-June, 1959.

This therapy proved effective in 51 cases of various inflammatory processes of the anterior structures of the eye. The medication was administered every four hours in the form of ointment. Almost every form of conjunctivitis, keratitis, and iritis is described and tabulated.

E. M. Blake.

Harrington, R. W. **Radiation damage to the chiasma and hypothalamus.** Tr. Ophth. Soc. U. Kingdom **78**:179-189, 1958.

Since the report of Beatson in 1896 that the development of certain cancers depends on hormones and that mammary cancer is affected by removal of the ovaries, hypophysectomy has been introduced. The author discusses the indications for such treatment and records the visual loss which resulted. Reports of the results and complications after the use of radon implants into the chiasm for pituitary ablation are given. An apparatus was devised to keep the patient's head fixed while under light anesthesia and a trochar and cannula had been inserted into the nostril under X-ray observation. Radon seeds of 10 to 20 mc were introduced into a definite area of the chiasm.

The effect of radiation on nerve tissue is a fibrinoid degeneration of the smaller blood vessels and subsequent demyelinization of the nerve cells. All defects resulting from radar progressed to total blindness. Diabetes insipidus coincidence was high. (19 figures)

Beulah Cushman.

Karpe, Gösta. **Indications for clinical electro-retinography.** Tr. Ophth. Soc. U. Kingdom **78**:373-390, 1958.

The clinical electro-retinography (ERG) represents the electric response of the retina under standarized conditions of dark adaptation, to single flash stimulation. A normal ERG consists of a negative deflection of the a-wave, and a large positive b-wave. In pathologic conditions four types are recognized and Karpe reports his findings in 3,500 examinations made for diagnosis and prognosis. (15 figures) Beulah Cushman.

Ley Gracia, A., Palomar Collado, F., Jacas Ejarque, R., Rovira Molist, M. and Palomar Petit, F. **A preliminary report on the diagnostic possibilities of cerebral angiography in orbital lesions.** Arch. Soc. oftal. hispano-am. **19**:294-300, April, 1959.

Three clinical cases of unilateral exophthalmos are reported to illustrate the value of angiography of the internal carotid artery in patients with orbital and periorbital neoplasms and vascular abnormalities. In two cases angiography led to the diagnosis of an intraorbital tumor, and in one it demonstrated an arteriovenous aneurysm of the lacrimal artery. Angiography visualizes the ophthalmic artery in 98 percent of cases; in 87 percent the ophthalmic artery can be followed to its small branches, visualizing in semilunar form the choroid plexus in the two posterior thirds of the orbit. (7 figures, 5 references) Ray K. Daily.

Lockwood, P. **New needle-holder for corneal suturing.** Brit. J. Ophth. **43**:442-443, July, 1959.

Lockwood describes a new needle holder in which there are two joints ra-

ther than one, adding much steadiness to the lower jaw of the instrument. It is particularly recommended for corneal suturing with the idea of preventing the lower jaw from slipping into the corneal wound when the needle is released. (3 illustrations) Morris Kaplan.

Malbrán, E. **Lateral mirror attachment for the Schepens ophthalmoscope.** Arch. oftal. Buenos Aires **33**:163-164, July, 1959.

A special mirror attachment for the Schepens binocular ophthalmoscope was devised in order to let a second observer get a view of the fundus. The mirror, which forms a 45-degree angle with the observation axis, reflects 60 percent of the light, 40 percent of which thus reaches the main examiner's eyes. It is hoped that with a Minox camera, mounted on a collapsible bracket, photographs of the fundus will be taken. (5 figures)

A. Urrets-Zavalía, Jr.

Mikuni, M. **A method to measure width of retinal vessels.** Klin. Monatsbl. f. Augenh. **135**:205-211, 1959.

A device was designed which can be attached to the Gullstrand ophthalmoscope and permits exact measurement of structures in the fundus. A description of the apparatus and its application is given, as well as methods for computing absolute values. (5 figures, 4 tables, 12 references) Gunter K. von Noorden.

Nelken, E. **Luminous frame for retinoscopy.** Brit. J. Ophth. **43**:444, July, 1959.

The author describes briefly a trial frame on which the degrees are marked in luminous paint to enable the retinoscopist to read the angle of the astigmatic band directly. (1 figure)

Morris Kaplan.

Ridley, Frederick. **Rational use of topical antibiotics in ophthalmology.** Tr. Ophth. Soc. U. Kingdom, **78**:335-358, 1958.

Human tears have the power of dissolving test organisms. Fleming, Allison and Ridley (1928) showed that normal whole tears are bactericidal for many strains of pathogenic staphylococci, streptococci and pneumococci. Any antiseptic substance to be effective in the conjunctival sac must fulfill these considerations: 1. must destroy the infecting organisms, 2. must inhibit growth of bacteria for a sufficient period, 3. must not be so destructive of the natural protective agent as to give rise to increased bacterial growth, 4. it must not inhibit the secondary natural defense mechanism, and 5. it must not be rendered ineffective by pus or serum in the conjunctival sac. It is suggested that drops at maximum concentration given four times a day and not at all during the night for seven days or less may secure the best conditions for combating a susceptible infection. (5 figures) Beulah Cushman.

Ridley, F. **Application for irradiation of the conjunctival sac.** Tr. Ophth. Soc. U. Kingdom, **78**:171-178, 1958.

A technique is described by which the control of radiation treatment of lesions of the conjunctiva and lids has been improved. An individually-fitted shell to carry radio-active foil or wire a predetermined distance from the eye or tissues is used. The immediate and remote effects of known dosages of gamma radiation is shown. Beulah Cushman.

Sampaolesi, R. **A device for anterior segment and chamber angle photography.** Arch. oftal. Buenos Aires **33**:165-166, July, 1959.

A 35-mm. reflex (Contaflex) camera with Compur shutter was adapted to one ocular of the Goldmann microscope; observation and focusing were made through the camera viewfinder and lens. While for large sections with the slitlamp the normal tension of 6 volts was used, a

moderate surcharge of the bulb (8 volts) was required whenever very fine sections were to be recorded. With film-speed ratings of 40 to 80 A.S.A., exposure times of 1/30 to one second were needed according to the width of the light beam, both for color and for black and white. (1 figure) A. Urrets-Zavalía, Jr.

Savin, L. H. **Intra-cranial aneurysms.** Tr. Ophth. Soc. U. Kingdom **78**:315-334, 1958.

Aneurysms rather than tumors may be suspected when there is more severe pain, sudden fluctuation in the visual fields, or ocular palsy. Fifth nerve irritation may cause intense tic douloureux in the ophthalmic division. Auditory sensation may be affected if part of the carotid in the bony canal is involved. Angiography is of great help and can be used without hesitation.

Ophthalmic migraine consists of hemicrania followed by paresis of the third, fourth and occasionally the seventh cranial nerve. The same side is usually affected in successive attacks. Pareses are often found associated with aneurysm of the internal carotid or posterior communicating arteries. Some of the patients develop subarachnoid and subhyaloid hemorrhages. Thrombosis of the posterior cerebral artery causes hemianopia in the contralateral half of the visual field and vascular lesions are recognized by the sparing of the macular vision. Local ocular lesions include spasm of the central retinal artery, vitreous hemorrhage and macular hemorrhage in myopia. (2 figures) Beulah Cushman.

Stepanik, J. **Photography of optical sections with the slitlamp.** Klin. Monatsbl. f. Augenh. **135**:259-263, 1959.

A photographic device is described which can be attached to the Haag-Streit slitlamp and operates with the utilization of two electronic flashes. This method enables the taking of perfect color photographs of the optical section. (6 figures, 8 references) Gunter K. von Noorden.

6

OCULAR MOTILITY

Alajmo, A. and D'Esposito, M. **Relation of eccentric fixation to the age of onset in the treatment for strabismus.** Arch. di ottal. **63**:227-232, May-June, 1959.

To prevent the development of amblyopia ex anopsia and anomalous fixation, complications which make orthoptic treatment so much more difficult, one should straighten crossed eyes before the age of three years. The incidence of these complications in 200 patients, aged 6 months to 6 years or over, is discussed. (1 table, 8 references.) Paul W. Miles

Arruga, Alfredo. **The vertical displacement of the horizontal recti.** Arch. Soc. oftal. hispano-am. **19**:269-281, April, 1959.

The literature on the correction of vertical phoria by raising or lowering of the vertical level of the horizontal rectus muscles during the course of an operation on these muscles for strabismus is reviewed. Hugonnier's theories are discussed in detail. The author's own material comprises 31 cases among 925 cases of strabismus in which this procedure was indicated. A tabulated report of these 31 cases gives data on the preoperative deviation, type of surgery, the postoperative result, the goal of surgery (esthetic or orthoptic) and pertinent observations. Ray K. Daily.

Dal Fiume, E. and Cordi, G. **Concomitant strabismus and anomalies of fixation.** Rassegna ital. d'ottal. **28**:216-233, May-June, 1959.

In the first portion of the article the authors review the theories concerning the anomalies of fixation and report the values of the incidence in diverse types of

fixation in 224 patients. Macular fixation was present in 16 percent, excentric in 10 percent, wandering in 10 percent, and double fixation in 4 percent. The various data revealed that the grave anomalous fixation is most often seen in the first year of life. The application of pleoptic and orthoptic treatment gave good results in poor macular fixation and almost none in the absence of fixation. E. M. Blake.

Ginsborg, B. L. and Maurice, D. M. **Involuntary movements of the eye during fixation and blinking.** Brit. J. Ophth. **43**: 435-437, July, 1959.

A method for determining the rapid movements of the eye during fixation and blinking is reported. These movements are made apparent by viewing a slow running time-base on the face of a cathode-ray oscilloscope while the gaze is fixed on a vertical trace 5 to 10 cm. in length and of spot velocity of 50 cm./sec. at a distance of 1 to 2 meters. The deviations are usually a rapid movement away from the line followed by a slightly slower return; they occurred at an average rate of two to 40 per minute and had a duration of 10 to 30 m.sec. They occurred both horizontally and vertically and were found to be independent in the two eyes. (2 figures, 7 references) Morris Kaplan.

Lesage, D. **Intermittent divergent strabismus.** Ann. d'ocul. **192**:751-779, Oct., 1959.

The author follows the classical division of intermittent exotropia into three groups: the primary convergence insufficiencies, the primary divergence excesses and the combined group where a convergence insuffiency is secondary to a primary divergence excess.

All cases with a divergence of greater than 20^{Δ} should have surgery. In cases of convergence insufficiency with less than this deviation orthoptic exercises alone will suffice. On the other hand, in divergence excess, surgery is the treatment of choice and the preferred procedure is a bilateral recession of the lateral rectus muscles. Patients with both a convergence insufficiency and divergence excess also require surgery but here a combination of recession and resection is indicated. (35 references) David Shoch.

Matteucci, P. **The sensory and motor symptoms of strabismic amblyopia.** Rassegna ital. d'ottal. **28**:161-168, May-June, 1959.

The author is convinced that the treatment of strabismus must above all be oriented to the reeducation of the motor component. Prolonged attention to the problem of the separation of the images, of the defects of fixation and of spatial localization is indispensible in attaining good results. By such treatment satisfactory results are generally obtained.
E. M. Blake.

Meesman, A. **Transplantation of the superior oblique muscle in complete oculomotor paralysis.** Klin. Monatsbl. f. Augenh. **135**:247-252, 1959.

In this operation recession of the lateral rectus muscle is followed by detachment of the medial rectus from the globe and suturing of the superior oblique to the sclera at the original insertion of the medial rectus after the tendon of the former has been shortened. The medial rectus is reattached to the sclera in an advanced position. The operation was successfully performed in four cases. The cosmetic result was furthermore improved when a ptosis procedure after Friedenwald was carried out in addition to the transplantation. (3 figures, 3 references) Gunter K. von Noorden.

Montanelli, M. **External rectus paralysis following the administration of antitetanus serum.** Boll. d'ocul. **37**:793-795, 1958.

The author reports a case of complete paralysis of the external rectus muscles following the administration of antitetanus serum. Complete restoration of function returned in about ten days. (3 references) Joseph E. Alfano.

Pagani, L. A. **A simple device for autoregistration of diplopia.** Rassegna ital. d'ottal. **28**:234-237, May-June, 1959.

Pagani reviews the numerous devices for the detection and study of diplopia, among them the Maddox rod, the Stevens test, Lancaster's red-green test and the diploscope. The author describes in detail the construction of an apparatus based on the reflection of images and finds it especially valuable from a medicolegal standpoint. (2 figures) E. M. Blake.

Rodriguez, L. **Hereditary congenital external ophthalmoplegia.** Arch. chil. de oftal. **15**:117-119, July-Dec., 1958.

The author presents the genealogic relationship among four individuals in two generations with congenital external ophthalmoplegia with ptosis and total immobility of the eyes. (1 figure, 6 references) Walter Mayer.

Verzella, M., Graziani, W. and Dal Fiume, E. **Eight cases of ocular torticollis.** Ann. d'ocul. **192**:736-750, Oct., 1959.

The authors describe eight cases of torticollis associated with vertical muscle anomalies. In three of the patients correction of the vertical anomaly also straightened the head tilt. It appears that the favorable preoperative factors are a large vertical component with a modest horizontal deviation and the presence of at least simultaneous perception. (8 figures, 41 references) David Shoch.

Walsh, Frank B. **The extraocular muscles in systemic diseases.** Arch. chil. de oftal. **15**:86-101, July-Dec., 1958.

This is a preliminary study, dealing with alterations found in the extraocular muscles in various systemic diseases such as inflammation, parasitic disease and metabolic disturbances degenerations and collagen diseases. The author concludes that many different diseases may produce similar muscle changes. Often there are no specific histologic changes in the muscles and a biopsy may not be representative of the histologic picture in the entire muscle. (28 references) Walter Mayer.

7

CONJUNCTIVA, CORNEA, SCLERA

Cremona, A. and Alezzandrini, A. A. **Treatment of corneal and limbal tumors by means of conjunctivo-sclero-keratoplasty.** Arch. oftal. Buenos Aires **33**:189-197, Aug., 1959.

Twelve patients with corneoscleral growths were successfully operated upon with a technique consisting mainly of a lamellar resection of the affected cornea and sclera with excision of the overlying conjunctiva, followed by transplantation of an identically sized and shaped fragment taken from a cadaver's eye. Of the six eyes of which a pathologic study was made, five had some kind of a malignant, epitheliomatous lesion and one only an epibulbar dermoid. All twelve patients were cured, with mostly good visual results; in one, however, a recurrence had to be followed by reoperation. (28 figures, 1 reference) A. Urrets-Zavalía, Jr.

Gedda, A., Bruna, F. and Magistretti, S. **The genetic etiology of keratoglobus.** Boll. d'ocul. **37**:735-753, Oct., 1958.

The author reports a case of keratoglobus occurring in a patient whose mother and perhaps an aunt were similarly affected. They discuss some of the hereditary features of this condition. (12 figures, 30 references) Joseph E. Alfano.

Günther, G. and Gebhardt, J. C. **First clinical experiences and histological examinations concerning frozen dehydrated corneal material for corneal grafts.** Acta ophth. **37**:241-252, 1959.

Lyophilized human cornea was used for lamellar grafts in six eyes. The donor material behaved unsatisfactorily; massive infiltration with round cells developed between it and the tissue of the host. Tissue cultures showed that no growth was obtainable in lyophilized corneal material of various species, and histologic examination confirmed the observation of death of the cellular elements. (10 figures, 12 references) John J. Stern.

Hallermann, W. **Various items on keratoplasty.** Klin. Monatsbl. f. Augenh. **135**:252-259, 1959.

The author records favorable experience with suture material obtained from rat tail tendons. Mattress type of sutures are preferred to hold the graft in place. In lamellar transplants a full thickness graft is sutured to the recipient cornea. This creates more favorable optical conditions because of less stromal scarring. A new thermos container for transportation of donor eyes is described. (6 figures, 5 references) Gunter K. von Noorden.

Marin-Amat, M. **Variations in corneal curvature during an ophthalmometric examination.** Arch. Soc. oftal. hispano-am. **19**:261-268, April, 1959.

The author refers to his former publications on this subject and discusses the etiology of transitory changes in corneal astigmatism in detail. The causes of such changes are extrinsically the action of the lids and extraocular muscles, and intrinsically the corneal elasticity, the effect of the ciliary muscle on Descemet's membrane and the increase in the size of the globe. After an analysis of the mechanism of these factors the author concludes that the transitory variations in the ophthalmometric data are caused by the rapid, automatic, and unconscious contractions of the orbicularis of the lids. This phenomenon also explains the rare refractions in which the axis and strength of the cylinder appear to vary from one moment to another.

Ray K. Daily.

Remler, O. **Familial occurrence of recurrent corneal erosion and its therapeutic management.** Klin. Monatsbl. f. Augenh. **135**:263-270, 1959.

Recurrent corneal erosion occurred in two children of the same family. The lesions responded well to treatment with ointments containing vitamin combinations. One cornea, however, was cauterized with a 20-percent solution of zinc sulfate. Not only did this treatment lead to increase of stromal edema and enlargement of the corneal lesion, but the author observed also subsequent development of Vogt's cataract in this eye. The etiology of Vogt's cataract is discussed in this connection. (2 figures, 6 references) Gunter K. von Noorden.

Vancea, P. **The oculo-ureturo synovial syndrome.** Ann. d'ocul. **192**:780-787, Oct., 1959.

A man, aged 39 years, was seen with the characteristic triad of Reiter's syndrome. The complete syndrome returned after a six-year interval with the addition of a unilateral iritis. The patient responded well to aureomycin therapy. (12 references) David Shoch.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Gross, A. G. **Treatment of uveitis.** Tr. Ophth. Soc. U. Kingdom **78**:207-25, 1958.

A full clinical examination after admission to the hospital is followed by bed rest, during which time a complete in-

vestigation of etiology is carried out. Routine tuberculosis chemotherapy in the form of isoniazid and para-amino salicylic acid is given and sometimes streptomycin cortisone drops are instilled into the eyes every two to four hours and mydriatics are instilled once or twice a day. If there is no contraindication adrenocortical hormones are prescribed in the form of prednisolone 15 mg. daily for three weeks, then 10 mg. daily for three weeks, then 5 mg. daily for two or three weeks and during that time 7½ grains of potassium chloride are given daily to assist in maintaining the electrolyte balance. Weight and blood pressure are to be checked twice a week.

With the absence of inflammation at the end of the course of treatment the medication can be stopped except for the topical application of the cortisone drops every four hours which should be continued through several months. If active inflammation persists, further systemic cortical hormones should be given before the dosage is gradually reduced.

The author has found that the treatment does not help in Behçet's disease but that it is of great help in sarcoidosis, sympathetic ophthalmia and toxoplasmosis when combined with daraprim and sulphanilamide. (3 tables)

Beulah Cushman.

9

GLAUCOMA AND OCULAR TENSION

Bitran, D. and Arentsen, J. **Comparative campimetry in chronic simple glaucoma.** Arch. chil. de oftal. **15**:104-112, July-Dec., 1958.

The authors review briefly the history of visual field examinations. They tabulate their findings in doing perimetric and campimetric studies in 50 glaucoma patients. Each patient was tested with three different perimeters (Goldmann, Etienne and Universal) and three campimetric studies were done on each patient with the Goldmann, the Etienne and the Bjerrum screen. They feel that among perimeters the Goldmann gives the most reliable results and that it is also this instrument which gives the most reliable results in campimetry. (3 tables, 15 references)

Walter Mayer.

Boles Carenini, B. **Lawford's syndrome.** Boll. d'ocul. **37**:767-775, Oct., 1958.

The author presents a case of bilateral Lawford's disease in a 43-year-old white man with bilateral facial naevi and bilateral chronic simple glaucoma without neurologic signs. There was no enlargement of the eyeballs and the glaucoma in the right eye was far advanced whereas that in the left eye was in the earliest stages. Both eyes showed increased scleral rigidity and reduced coefficient of facility of outflow. The author felt that the latter factor was responsible for the glaucoma. (2 figures, 30 references)

Joseph E. Alfano.

Gormaz, A. **Medical-surgical corroboration of the hypotensor mechanism of peripheral iridectomies in angle closure glaucoma.** Arch. chil. de oftal. **15**:120-122, July-Dec., 1958.

In a patient with glaucoma who had had repeated iridosclerectomies and peripheral iridectomies done gonioscopic examination showed that some of the iridectomies did not encompass the entire thickness of the iris; as soon as one was performed which removed part of the entire thickness of the iris the tension became normal.

Walter Mayer.

Koskenoja, M. and Suvanto, E. **Gargoylism. Report of adult form with glaucoma in two sisters.** Acta ophth. **37**:234-240, 1959.

Gargoylism was observed in two sisters aged 44 and 55 years; both had bilateral glaucoma. (6 figures, 1 table, 40 references)

John J. Stern.

Lester, A. **Observation on some results of perforating cyclodiathermy.** Tr. Ophth. Soc. U. Kingdom **78**:191-205, 1958.

The author feels that the problem of the treatment of primary congestive glaucoma is largely solved with use of eserine, diamox, wide iridectomy and iris inclusion. In chronic simple glaucoma the outlook is different. Potential trouble remains in glaucoma in the elderly in the colored races, in the aphakic eyes, in eyes with incipient lens opacities and in eyes in which medical and surgical treatments have failed.

Perforating cyclodiathermy may be done through the intact conjunctiva but the author prefers to expose the sclera and make about thirty applications with a 1.0 mm. electrode on two rows 8 and 6 mm. from the limbus on either side of the inferior rectus muscle using a current of 70 m.a. for four seconds. In 33 patients with all types of glaucoma he reports better than usual results. He feels that perforating cyclodiathermy is more effective than surface cyclodiathermy. It does have a temporary effect but can be repeated. The effect of cyclodiathermy is due to ischemia and its effect may be made to last longer by employing local cortisone. (8 tables) Beulah Cushman.

Leydhecker, W. **The social significance and frequency of glaucoma.** Klin. Monatsbl. f. Augenh. **135**:188-196, 1959.

Glaucoma is in many countries the most common cause of blindness. Patients with glaucoma simplex are frequently seen for the first time at a stage where the disease is already too far advanced for effective therapy. Stimulated by similar population studies in the U.S.A. the author measured ocular tension with the Schiøtz tonometer in 10,000 individuals who had no ocular complaints and were considered healthy. In persons with a scale reading of 3.5 (5.5 Gm. weight) or lower, perimetry, tonography, ophthalmoscopy, and biomicroscopy were performed. Glaucoma was diagnosed when marginal excavation and atrophy of the disc was present, or when the visual field studies revealed temporal extension of the blind spot. A scale reading of 2.5 (5.5 Gm. weight) was considered to be pathologic provided scleral rigidity was normal. After the fourth decade glaucoma was diagnosed in 2.3 percent of the individuals who were examined. This figure coincides exactly with results obtained from similar studies in this country. Glaucoma simplex was also found in people younger than 40 years. Increase in intraocular pressure preceded field loss for many years. The author concludes from this that pressure increase is the main etiologic factor for field loss. In several instances a hereditary pattern of glaucoma simplex and in some cases unilateral occurrence were discovered in this study. (2 figures, 10 references, 1 table)

Gunter K. von Noorden.

Linner, E. and Wistrand, P. **The initial drop of the intraocular pressure following intravenous administration of acetazolamide in man.** Acta ophth. **37**:209-214, 1959.

Using repeated short applications of the tonometer in normal human eyes, a pressure drop was found to take place within the first two minutes after intravenous injection of acetazolamide. No drop was recorded when the tonometer was kept on the eye continuously. This discrepancy cannot be explained at present and deserves further study. (4 figures, 15 references) John J. Stern.

Nordmann, Jean. **Fundamental questions concerning glaucoma.** Ann. d'ocul. **192**:572-591, Aug., 1959.

This is the second part of a two-part article. In the previous paper the author concluded that the origin of the increase in ocular tension in glaucoma was ocular and not in the central nervous system. In the present article he discusses defects

of the optic nerve and visual field in glaucoma. The optic nerve atrophy in glaucoma is of two types: 1. a simple Wallerian degeneration due to injury of the cell body and 2. a cavernous atrophy which never extends centrally beyond the point of entrance of the central vessels. The latter is not specific for glaucoma. In either case, from the point of view of the optic nerve, glaucoma is a disease of the eye and not of the central nervous system.

The author then considers the evidence for a posterior etiology for the visual field defects seen in glaucoma. He concludes that if there were a hypothalamic center involved, the field defects should be of the homonymous hemianopic type. Since they are frequently unilateral or bitemporal, the defect must originate in the globe or near it. He concludes therefore, on the basis of the ocular tension, the optic nerve atrophy and the field defects, that glaucoma is a disease of ocular origin. (191 references) David Shoch.

Pierce, Darmot. **A method of inclusion.** Tr. Ophth. Soc. U. Kingdom **78**:223-226, 1958.

Iris inclusion is a widely performed operation for glaucoma and the author feels that the technique as used at the Croyden Eye Unit is relatively easy to perform. The iris forceps is introduced into the anterior chamber through an ab externo incision made tangentially instead of towards the pupil. The iris is grasped and withdrawn into the incision by tearing it at its root. The tongue of iris is incised by a single lateral cut. (3 figures)

Beulah Cushman.

Primrose J. **The priscol test in glaucoma.** Tr. Ophth. Soc. U. Kingdom **78**: 261-265, 1958.

Subconjunctional injection of priscol as a provocative test in chronic simple glaucoma was done on 32 patients in whom the results of the water drinking and tonography tests were available; the priscol test was positive in 80.5 percent using 9 mm. as positive. The average rise in tension was 12.00. Six patients with chronic glaucoma were tested to exclude the narrow-angle factor.

Priscol is a vasodilator and probably raises the tension by increasing the production of aqueous. The normal eye can adjust to the increase but the glaucomatous eye fails to do so. Gonioscopy performed before and during the test showed no change in the state of the angle.

Beulah Cushman.

Sampaolesi, R. and Reca, R. **Protracted tonography.** Arch. oftal. Buenos Aires **33**: 155-162, July, 1959.

If, following Leydhecker's directions, tonography is performed over a seven-minute, instead of the usual four-minute period, and only the three to seven-minute part of the curve taken into account, more accurate information is gathered as to the real value of the coefficient C. This is due to the fact that only after the third minute does the intraocular pressure fall in a linear fashion, a steady-state being achieved once the initial marked drop due to the elastic distension of the eyeball has ceased to act as a disturbing factor. This, of course, has nothing to do with any possible abnormality of the scleral rigidity, which, if present, would lead to large errors unless properly assessed and corrected. The significance of individual figures may still be increased if in lieu of the coefficient C, the fraction Po/C (Abflusswert) is taken as an index of the facility of outflow.

A group of 50 normal, and one of 67 confirmed glaucomatous eyes were submitted to this test. The results, stated in terms of the mean values obtained for C_{0-4} and C_{3-7}, were of 0.31 ± 0.105 and 0.17 ± 0.057 for the former series, and of 0.11 ± 0.080 and 0.06 ± 0.030 for the latter

one. The degree of probability for a given reading to have a pathologic significance was calculated on the basis that C values lower than M-1σ would already be suggestive of glaucoma, and that C values lower than M-2σ should be considered sure proof of an abnormally decreased outflow. As, however, it is generally accepted that only for values lower than M-2σ and M-3σ, respectively, could such an interpretation be valid, the author's claims as to the high percentage of cases where a definite diagnosis of glaucoma could be made by tonography alone, must be regarded with extreme caution.

Although the mean values of Po/C_{0-4} and Po/C_{3-7} are given as being normally of 52 and 57, no data as to how the standard errors for both these figures were obtained are given. (2 tables, 2 graphs, 15 references) A. Urrets-Zavalia, Jr.

Simonett, B. **The brachial blood pressure and its relation to the course of glaucoma simplex.** Klin. Monatsbl. f. Augenh. 135:196-205, 1959.

A number of factors which may be contributory to the development of primary glaucoma are listed. A comparative investigation was carried out on 232 patients who had glaucoma simplex or chronic cyclic glaucoma. The systolic and diastolic blood pressure as measured at the brachial artery was correlated with the course of the ocular disease. A constant relation between the brachial blood pressure and clinical course of the glaucoma, or between ocular tension and brachial pressure could not be established. (5 figures, 2 tables, 9 references)

Gunter K. von Noorden.

Smith, Redmond. **The incidence of the primary glaucoma.** Tr. Ophth. Soc. U. Kingdom 78:245-295, 1958.

The author became interested in the incidence of the types of primary glaucoma; 608 patients were examined at the glaucoma clinic and divided into groups A and B. Group A comprises the cases of known or suspected primary glaucoma; Group B consists of all the other cases.

Classification was based on an assessment of the clinical features, combined with gonioscopy, tonometry and fundus examination. Visual field studies were made only where helpful for diagnosis, and provocative and outflow tests were done when indicated. Group A had 506 cases of which 386 were simple glaucoma, 209 were closed-angle glaucoma; 134 chronic simple glaucoma; and 25 of an unknown type. Of the 102 cases in Group B 66 were primary glaucoma, 48 were closed-angle; 16 were simple glaucoma; 2 were of an unknown type. In each group about one fourth of the patients were male. (9 tables)

Beulah Cushman.

Sveinsson, K. **Glaucoma and heredity in Iceland.** Acta ophth. 37:191-198, 1959.

Of 1,561 glaucoma patients in Iceland, 15 had secondary glaucoma and 1,544 primary (90.29 percent glaucoma simplex, 7.9 percent chronic inflammatory, 1.81 percent acute). Males are affected almost twice as frequently as females. Among the patients with primary glaucoma, 724 had close relatives who had glaucoma. The disease appears mainly at the ages between 60 and 90 years, and heredity seems to be mainly dominant.

John J. Stern.

Vena Rodriguez, Antonio. **Ganglioplegics in glaucoma.** Arch. Soc. oftal. hispano-am. 19:305-308, April, 1959.

A brief review of the literature on the action of ganglioplegics is followed by a report of five cases of glaucoma in which miotics failed to reduce a high intraocular pressure and the retrobulbar injection of 15 to 25 mg. of pendiomid brought the tension down to safe limits. One of these patients had acute glaucoma, one had

glaucoma secondary to traumatic cataract, and one was diabetic and had hemorrhagic glaucoma. Ray K. Daily.

10
CRYSTALLINE LENS

Amaral Filho, A. and Tupinanba, J. **Symposium on the pathology of the crystalline lens.** Arq. brasil. de oftal. **21**:392-425,1958.

Amarel, F. **Congenital and acquired anomalies,** pp. 392-419.

Congenital anomalies of the lens may occur in various forms, affecting the size, shape, position and transparency. The most commonly observed are aphakia, microphakia-spherophakia, coloboma, lenticonus, ectopia, congenital cataract, persistence of the hyaloid artery and pseudoglioma. Acquired anomalies may affect the position of the lens, cause changes in the capsule and capsular epithelium, or opacities within the lens substance. Each of these anomalies is discussed briefly, with a review of the signs and symptoms of cataract. The various types of cataract are summarized. (8 references)

Tupinanba, J. **Physics, chemistry and physiology of the pathological crystalline lens.** pp. 419-425.

In this, the second chapter on pathology of the crystalline lens, the author reviews the literature on the physical and chemical properties of the lens. He mentions a possible diagnostic sign of early cataract formation in the diabetic—a fluorescence more intense than is normally observed with a greater percentage of radiations in the blue spectrum. There is a discussion of the protein metabolism, mineral content, oxidation and reduction and other aspects of lens physiology. (8 references)

James W. Brennan.

Auricchio, G. and Testa, M. **The content of glaucosamine in human senila cataract.** Rassegna ital. d'ottal. **28**:99-101, March-April, 1959.

Following a study of the content of glaucosamine in the lens of rabbits and oxen the work was continued in man. The patients were from 50 to 75 years of age and the cataracts were removed in capsule and were immediately immersed in Thunberg solution. The chemistry involved is elucidated. Cataract is very rich in glucosamine which is lacking in the normal lens. It seems probable that the process is a simple diffusion from the surrounding fluid and altered permeability of the capsule. E. M. Blake.

Barreau, R. **A new technique of suturing for cataract surgery.** Arch. chil. de oftal. **15**:123-126, July-Dec., 1958.

The author described his technique of placing track sutures, in which the suture has been stained in methylene blue, and therefore leaves a well stained track which does not spread like fluoresceine and does not wash out easily, but disappears after 24 hours. The methylene blue gives good enough visibility for recognition of perfect apposition. The author uses five corneo-scleral sutures. (2 figures)

Walter Mayer.

Bosso G. **Hemorrhage into the anterior chamber after extraction of cataract.** Rassegna ital. d'ottal. **28**:204-215, May-June, 1959.

The causes of hemorrhage into the anterior chamber are studied from all angles. The reasons why some hemorrhages occur during the operation, some a few hours later and some not for several days are considered. The female is more predisposed than the male. The presence of diabetes and degenerative vascular changes as well as glaucoma, myopia, old iritis or uveitis, trauma and the presence of adrenalin in the local anesthetic are factors predisposing to hemorrhage. After absorption of the hyphema the visual acuity varies from nil to 20/40.

E. M. Blake.

Casero, L. **Enzymatic zonulosis.** Arch. Soc. oftal. hispano-am. 19:301-304, April, 1959.

The author's material comprises 53 cases, ranging from a traumatic cataract in an 18-year-old boy to cortical cataracts in a woman who was 83 years of age. Adhering to Barraquer's technique the author encountered no complications, except for delayed reformation of the anterior chamber with a moderate choroidal detachment in three patients. In one of them the anterior chamber remained flat for 20 days; it finally reformed without surgery and no postoperative complications developed during a period of observation of four and one half months. Diamox proved ineffective in these three patients; in one a compressive bandage was followed after 24 hours by restoration of the anterior chamber. Ray K. Daily.

Keerl, G. **Late total opacity of partial traumatic cataract.** Klin. Monatsbl. f. Augenh. 135:274-278, 1959.

The medicolegal problem of late opacities occurring in lenses previously injured is discussed. A patient developed intumescent cataract 29 years after the lens was traumatized by a perforating injury. According to Vogt, late opacities occur only as a result of a capsular tear, therefore direct or indirect evidence of capsular rupture or the presence of a scar is required for approval of compensation in such a case. Development of rapidly progressing intumescent cataract leading to complete opacity speaks in favor of its traumatic origin. (13 references)

Gunter K. von Noorden.

Liegl, O. **Experiments with zonulolysis in cataract operations.** Klin. Monatsbl. f. Augenh. 135:241-246, 1959.

The author compares 113 cataract extractions made with zonulolysis by trypsin or alpha-chymotrypsin and 113 extractions without employment of the enzyme. Zonulolysis facilitates intracapsular extractions, shortens the procedure, and reduces the operative and postoperative complications. A damaging effect of the enzymes on ocular tissues other than on the zonules was not observed. Trypsin and alpha-chymotrypsin were found to be equally effective and compatible. Younger patients especially benefit greatly from the advantages of enzymatic zonulolysis. (1 table, 7 references)

Gunter K. von Noorden.

Miller, Dorothy. **A case of anorexia nervosa in a young woman with development of subcapsular cataracts.** Tr. Ophth. Soc. U. Kingdom 78:217-222, 1958.

A young woman, aged 19 years, developed subcapsular cataracts when her weight was reduced as a result of no food plus the taking of bile beans. She showed no signs of vitamin deficiency and the extreme emaciation continued over a period of ten years. There were no skin lesions and no history of allergy, hayfever or asthma. (5 figures)

Beulah Cushman.

Pirodda, A. **Experimental cataract reduced by the use of antimytotic substances.** Boll. d'ocul. 37:717-726, Oct., 1958.

The author was able to produce cataracts in three-months-old rabbits by the systemic administration of colchicine and triethylene melamine. Several days after the administration of these substances histologic examination of the lens epithelium revealed that there was an increase of the number of cellular mitoses followed by a persistent decrease in the number of cellular mitoses. The lens opacities appeared about 20 to 30 days after the administration of colchicine and 60 to 70 days after the administration of triethylene melamine. The opacities at first appeared as punctate posterior polar cataracts which ultimately went on to complete opacification. (3 tables, 3 figures, 7 references) Joseph E. Alfano.

Rohrschneider, W. **Experiences with enzymatic zonulolysis in 320 cataract extractions.** Klin. Monatsbl. f. Augenh. 135:226-231, 1959.

A severely damaging action of the enzyme was not observed in any of the cases. It must be assumed, however, that alpha-chymotrypsin tends to decrease resistance to injury of the lens capsule in older persons and causes some damage to the anterior limiting vitreal membrane. The enzyme delays wound healing to some degree and this resulted in an increased occurrence of iris or vitreous prolapse. For this reason corneoscleral sutures are thought to be advisable. The enzyme facilitates intracapsular extraction. In juvenile cataracts zonulolysis should not be employed in patients under 10 years of age. (2 tables)

Gunter K. von Noorden.

11

RETINA AND VITREOUS

Espildora Luque, C. **A special variety of retinal detachment.** Arch. chil. de oftal. 15:102-103, July-Dec., 1958.

The author has seen three cases of a syndrome in which an emmetropic patient in middle age had a massive vitreous hemorrhage which cleared in an amazingly short time and was followed a few days later by a superior detachment which did not have any tendency to extend downward. The author points out that an eye with a rapidly-clearing vitreous hemorrhage should be thoroughly investigated as soon as possible because of the possibility of an upper detachment.

Walter Mayer.

Graham, P. A. **Unusual evolution of retinal detachments.** Tr. Ophth. Soc. U. Kingdom 78:359-370, 1958.

Two cases of retinal detachment are described in which the author noted holes followed within three weeks by acute hypotonia, uveal congestion, and a characteristic distortion of the iris due to retraction of the lens-iris diaphragm. (5 figures)

Beulah Cushman.

Jayle, G. E., Boyer, R. and Aubert, L. **Various electro-retinographic functional tests in severe senile macular degeneration.** Ann. d'ocul. 192:561-571, Aug., 1959.

In addition to standard electroretinography various other tests were made on four patients with senile macular degeneration. Records were obtained at various levels of dark adaptation, in red light and in response to flicker. The authors show that although the standard electroretinogram was normal in three of these patients, the remaining tests did reveal an abnormality of the retina. This injury is characterized by the very early disappearance or absence of A-1 waves, by absence of response to red stimuli, and by decreasing frequency of fusion. (15 figures, 24 references)

David Shoch.

Leisham, R. **Vascular changes in progressive failure of vision.** Tr. Ophth. Soc. U. Kingdom 78:303-314, 1958.

Vascular changes in the retina depend on the extent to which the flow of blood to the tissue is interfered with at any level of the vascular tree, modifying the circulation and so contributing to disorganization in the periphery.

Replacement fibrosis is a common cause of loss of reactivity both in arteries and arterioles. This process involves the replacement of cellular contractile elements in the vessel wall by inert collagen, diminishing reactivity and presumably increasing rigidity. Resilience may still be retained in the endothelium and it is conceivable that the endothelium could retract from a rigid portion of the wall in order to maintain a blood column of diminished volume. In this way, relative circulatory failure might initiate a chain of events leading to the development of

atherosclerotic occlusive lesions. Visual acuity is unaffected by involutionary sclerosis in the absence of complications but rapidly deteriorates with evidence of vascular disorganization in the fundus if the systolic blood pressure is lowered.

Diffuse narrowing of the retinal arteries is a rule when a younger vascular system is affected by high blood pressure. The author doubts that spasm plays an important part in vascular disorders of the retina. Thrombosis, more common in the terminal arterioles of the retina, occurs in fibrous and presumably rigid central arteries within the optic nerve and is usually secondary to some disorder of circulatory dynamics.

Senile macular degeneration is a cause of progressive failure of vision in old people. The histologic changes are those of advanced arterial fibrosis in the local vascular systems of the choroid and retina, but the effects of complete vascular breakdown are limited to the macular area of the retina. The condition is of gradual onset and soon affects both eyes. The effects of occlusive arterial lesions at regional and local levels depend upon the availability of collateral blood supplies.

Beulah Cushman.

Lorentzen, S. E. **Micro-aneurysms of unknown nature observed ophthalmoscopically.** Acta ophth. 37:279-289, 1959.

Solitary micro-aneurysms were observed in two healthy individuals and several in one with iron-deficiency anemia. (1 figure, 41 references)

John J. Stern.

Nicolato, V. **Tapeto-retinal degenerations and the effectivity of treatment.** Arch. di ottal. 63:281-336, July-Aug., 1959.

In this long review the author discusses retinitis pigmentosa and many other related diseases such as familial hemeralopia, retinosis punctata albescens, Oguchi's disease, and choroideremia. He concludes that no exact line of difference exists in individual cases. Transitional types are almost the rule. The symptoms common to all include hemeralopia, vasoconstriction, retinal and optic atrophy, dyschromatopsia, reduced central and peripheral vision, and reduced dark adaptation. No effective treatment has been developed. (41 references) Paul W. Miles.

Zeidler, I. **The clinical electroretinogram. IX. The normal electroretinogram. Value of the b-potential in different age groups and its differences in men and women.** Acta ophth. 37:294-301, 1959.

In the 31 to 50 year age group the b-potential is significantly larger in women. Statistically different values are also found in different age groups. (4 tables, 5 references) John J. Stern.

12

OPTIC NERVE AND CHIASM

Kjer, P. **Infantile optic atrophy with dominant mode of inheritance.** Acta ophth. Suppl. 54, 1959.

This large monograph deals with a type of infantile optic atrophy different from Leber's disease. The latter and two other types (congenital optic atrophy with dominant transmission and nystagmus, optic atrophy which is congenital or of early onset, with recessive transmission) are discussed. Infantile optic atrophy with dominant mode of transmission was observed in 19 Danish families with about 1,200 members. The condition was demonstrated in 200 subjects and probably present in an additional 49. In 98 cases where the results of earlier examinations were available the disease was progressive in 50 patients and stationary in 48. In the latter group the observation time was shorter. Visual acuity varied from normal to considerably, but not extremely, reduced values. Varying degrees of optic atrophy and, at times, cupping were ob-

served. The macula was normal in some subjects but frequently showed either an enlarged or an absent foveal reflex. In 15 cases some pigmentary changes were seen in the macula. Fields were examined in 102 cases; in 82 of them changes were found, never as pronounced as the central scotoma of Leber's disease, but ranging from an extension of the blind spot to a marked cecocentral scotoma. Color perception, particularly for blue, was frequently impaired. There was no night blindness, nystagmus or other evidence of a neurologic disturbance in the patients. The mode of inheritance is completely dominant and autosomal; 50 percent of the descendants of an affected mother or father were affected. These findings are correlated to the literature, and eugenic measures are discussed. The author recommends that requests for sterilization or abortion by affected parents should be complied with. John J. Stern.

Kreibig, W. **Aplasia and hypoplasia of the optic disc.** Klin. Monatsbl. f. Augenh. **135**:212-223, 1959.

Congenital defects of the optic disc in an otherwise normally developed eye are among the greatest rarities. The condition is less rare if associated with cranial malfunctions or microphthalmos. Bilateral congenital aplasia of the disc was found in an infant who suddenly died 34 hours post partum. With the exception of osteogenesis imperfecta no other systemic disease was found on autopsy and the death remained unexplained. A detailed pathologic-anatomical description of the eyes is given and an apparently isolated defect of the third retinal neuron was present involving ganglion cell and nerve fiber layer. The histological findings corresponded entirely with anatomical defects described in eyes of two anencephalic monsters and were similar to those seen in a third case of anencephalus. The clinical appearance of aplasia or hypoplasia of the disc is discussed and several cases are cited from the literature. The author divides papillary defects into three groups: 1. complete absence of the optic nerve and its blood vessels, 2. an isolated defect of the third retinal neuron while an optic nerve structure exists and the entry of the blood vessels into the nerve is normal, and 3. hypoplasia of the disc. (6 figures, 24 references)

Gunter K. von Noorden.

Stellamor-Peskir, H. **The treatment of acute disseminated chorioretinitis.** Ophthalmologica **137**:372-376, June, 1959.

The principle of the author's method of treating acute disseminated chorioretinitis is to use steroids by mouth in a dosage carefully adjusted to the course of the disease as observed with the ophthalmoscope. The first step is a thorough general examination including a specific search for diseases likely to be aggravated by steroids such as active tuberculosis, diabetes, gastrointestinal ulceration, and renal insufficiency. After these conditions have been ruled out steroids are started in the form of prednisone or prednisolone by mouth, in daily doses of 30 to 40 mg. Smaller initial doses have been ineffective in the author's experience. On these large doses the majority of the cases shows definite regression of the exudative process within the first two or three days. If such improvement fails to occur the author increases the oral dosage or adds hydrocortisone retrobulbarly in daily doses of 10 to 20 mg. Once a change of the ophthalmoscopic picture for the better is noted, the dosage of the steroids is slowly reduced. The total amount of prednisone or prednisolone given in one course of treatment is 200 to 250 mg. Just before stopping the oral therapy altogether the patient is given 40 units of ACTH (intramuscularly) twice, 24 hours apart.

A few of the author's patients showed no response whatsoever to the routine

steroid therapy. A strikingly positive response, however, was noted if streptomycin was added in the usual intramuscular doses. The author assumes different pathogenetic processes in the two groups of cases.

Most of the author's patients showed old choroiditic scars as well as acute chorioretinitic lesions. The latter, under the influence of steroid therapy, became transformed into finer, less pigmented scars than those that developed in the presteroid era. The degree and extent of choroidal atrophy, particularly, seemed to be considerably lessened by the steroid therapy.Thus, in the same eye, the observer was able to distinguish between scars which occurred before steroids were given and scars that formed under the influence of steroids.

Similar observations, that is lessening of the inflammatory reaction and finer, smaller scars, were made in rabbits in which choroiditic lesions were produced experimentally by means of electrocoagulation. (8 references) Peter C. Kronfeld.

Venturi, G. and Volpi, U. **Studies of the sensitivity of the retina in aphakic subjects.** Boll. d'ocul. 37 :706-713 ; Sept., 1958.

By means of a Goldmann-Weeker adaptometer, the dark adaptability of the retina, as well as the visual acuity at reduced illumination, were studied in uni- and bilateral aphakia. The authors found that there was a reduction in the retinal sensitivity to light as well as a modification of both the scotopic and photopic segments of the dark adaption curves. They also found that the visual acuity at reduced illumination was also reduced. They feel that these findings are due to the action on the retinal photoreceptors of certain light rays which would under normal conditions be absorbed by the lens. They also found that if an antiactinic filter was placed before the aphakic eyes during the preadaptation phase, both the dark adaption curves and the visual acuity would return to normal. (1 graph, 13 references)

Joseph E. Alfano.

Zeeman, W. P. C. **The prognosis of retinoblastoma in the Netherlands.** Ophthalmologica **137** :425-426, June, 1959.

Several years ago Weve suggested systematic follow-up of the decendants of retinoblastoma patients as a means of early diagnosis of the disease. A pilot study of the feasibility and of the implications of such an investigation was made by Dr. G. D. Hemmes. The principal results of this study are now reported by Zeeman. Early diagnosis and early treatment have undoubtedly increased the number of survivors among the retinoblastoma patients which implies an increased risk of transmission of the disease to subsequent generations and thereby a higher incidence of the disease. Actually, Dr. Hemmes' study reveals that the incidence of retinoblastoma in the Netherlands is rising and will continue to do so unless the descendants of retinoblastoma patients are observed more closely and advised and guided with regard to the status of the disease in their family. Hemmes estimates the risk of developing retinoblastoma as being about 50 percent in group I, that is all further children in generations in which two children already have retinoblastoma; as being 30 percent in group II which consists of patients with unilateral retinoblastoma, and as being 15.7 percent in group III which consists of the children of "isolated" retinoblastoma patients (without demonstrable hereditary background). Cousins of retinoblastoma patients are excellent risks.

The proper care and supervision of the descendants of retinoblastoma patients will require close cooperation between the general practitioner and the ophthalmologist, and frequent re-examinations of the eyes of the suspects under maximal mydri-

asis and, if necessary, under general anesthesia. Peter C. Kronfeld.

13

NEURO-OPHTHALMOLOGY

D'Esposito, M., Serra, C. and Ambrosio, A. **Recent acquisitions in neuro-ophthalmology (electromyography of the ocular muscles).** Arch. di ottal. **63**:183-210, May-June, 1959.

In this long paper 74 references, mostly to articles originating in the United States, are reviewed. Electromyography was shown to be important in studies of binocular physiology in health and in disease. It may determine the type of nystagmus, it may be a guide in the surgery of vertical muscles, and it may reveal the extent of ophthalmoplegia. Electromyography will show harmonic or subharmonic photic driving. Paul W. Miles.

Kojima, K., Natsume, C., Miyagawa, C. and Honda, A. **Papilledema caused by subdural hematoma.** Acta Soc. Ophth. Japan **63**:801-804, April, 1959.

A man, 25 years old, noted a disturbance of vision and concentric contraction of the visual field after cranial trauma. He had bilateral choked disc. Craniotomy was done and a subdural hematoma was found in the frontal lobe of the right side; its removal brought about improvement of the vision and visual field. (4 figures, 1 table, 3 references) Yukihiko Mitsui.

Manschot, W. A. **Embolism of the central retinal artery originating from an endocardial myxoma.** Ophthalmologica **137**: 430-431, June, 1959.

A 57-year-old male patient suddenly lapsed into a subcoma; on admission to the neurological department of a hospital in Rotterdam he was found to have a right-sided spastic hemiplegia including the right facial nerve. Ophthalmoscopically the right eye was reported as normal while the left eye showed papilledema and a recent inflammatory focus between disc and macula. The patient died three days later. Autopsy revealed a large area of encephalomalacia on the left side, involving the temporal and parts of the frontal and parietal lobes. The lumen of the left carotid artery, one and one half centimeters proximal to its opening into the circle of Willis, was completely filled with a yellow-red transparent mass which on histologic examination proved to be a part of a myxoma located in the left atrium. Similar emboli were found in the left central retinal artery and in one left posterior ciliary artery. Peter C. Kronfeld.

Seltzer, I. Rodenstein, J. and Zimman, L. **Spinocerebellar ataxia associated with macular dystrophy. Report of a case.** Arch. oftal. Buenos Aires **33**:85-89, June, 1959.

The case of a 19-year-old boy is presented in whom, in addition to some incoordination in the use of the arms and hands, scanning speech, and clumsiness in walking, an increase in the tendon reflexes and a marked spasticity of the lower limbs had developed during the last two years. There were also a horizontal nystagmus and a bilateral macular degeneration much reminiscent of that seen in Stargardt's disease. Vision was reduced to 0.1 in both eyes. The condition was considered to be representative of the Pierre Marie type of hereditary ataxia, although the fact that a pes cavus existed would suggest that it was in some way related to Friedreich's ataxia. It would be well to mention that some 27 cases of tapeto-retinal degenerations associated with the hereditary ataxias and allied conditions are to be found in the literature, in at least four of which the fundus changes were of the central, macular type (Sjögren, 1943: one case; Louis-Bar and Pirot, 1945: one case; Walsh, 1947: two cases in siblings). (2 figures, 17 references)

A. Urrets-Zavalia, Jr.

Walsh, Frank B. **Paratrigeminal syndrome of Raeder, regeneration of the third nerve, and subdural hematoma.** Arch. chil. de oftal. **15**:75-85, July-Dec., 1958.

Patients with Raeder's paratrigeminal syndrome have pain in and around one eye, ptosis, and miosis. The author describes some of the patients he has seen with severe headaches which pulsate and usually appear during the night and last until the next afternoon. These crises are repeated nightly but the severe pain usually subsides within two weeks. Shortly after the headache starts a homolateral ptosis begins and the pupil becomes miotic. After about one year the symptoms disappear. The author ascribes this syndrome to dilation of the wall of the arteries during the headache and if this persists for a long time the arterial wall becomes edematous. The oculo-sympathetic fibers are included in the internal carotid artery and their interruption will produce miosis and ptosis. (3 references)

Acquired paralysis of the third nerve may be due to aneurysm, trauma, tumors, diabetes, inflammation and ophthalmoplegic migraine and it is mainly in cases of aneurysm that regeneration of the third pair occurs. After regeneration there are a greater number of fibers than before and some areas which previously were not functioning will receive new axones in this aberrant regeneration. In such cases axones which previously went to the superior rectus now go to the levator and fibers from the medial rectus go to the inferior rectus or oblique muscles. These patients cannot move their eyes up or down, but are able to adduct or abduct. The lesions, once they are established, are permanent. There are, of course, cases in which the regeneration of the third nerve occurs in a normal fashion. (6 references)

The origin of subdural hematoma is trauma in early childhood, usually before 12 years of age. They are almost never found in subjects between 12 and 20 years of age. In adults alcoholism, syphilis and cortical atrophy are predisposing factors. The author notes the absence or paucity of neurologic signs and describes in detail such eye signs as papilledema, retinal hemorrhages, homolateral mydriasis, conjugate deviation, ptosis, paralysis of cranial nerves, nystagmus, optic atrophy, and changes in the visual field. Radiographic changes are also noted. (5 references) Walter Mayer.

14

EYEBALL, ORBIT, SINUSES

McLaren, L. R. **Early healing of the orbit after exenteration.** Tr. Ophth. Soc. U. Kingdom **78**:391-403, 1958.

Exenteration of the orbit is reviewed and the authors experience with 17 patients operated upon in the previous four years is reported. The fact that the procedure in the treatment of malignant tumors of the orbit or extensive disease of the eyelids is mutilating is a secondary consideration where treatment of malignant disease is concerned.

Early healing of the orbital wound and a life-like prosthesis fitted without delay removes the temptation to procrastinate.

A method for surgery and the after care are described in detail. The patients can leave the hospital in 10 to 14 days. (4 figures) Beulah Cushman.

Nover, A., Zielinski, H. W. and Josten, K. **Diagnosis and control of the clinical course of exophthalmos.** Klin. Monatsbl. f. Augenh. **135**:32-52, 1959.

Orbital compressibility was measured in 102 patients with orbital disease. A piezometer as described by Jaeger was used. In patients with orbital tumors the compressibility was lowered and directly dependent on the degree of exophthalmos present. Orbital inflammatory diseases gave varying results. Orbital tonometry aids in evaluation of the course of orbital

inflammation and its therapeutic management. Tumors and inflammations of the paranasal sinuses as well as growths in the sphenoid region gave variable results. Sudden changes in compressibility and distinct pulsations were the characteristic piezometer readings in pulsating exophthalmos. In endocrine exophthalmos little difference was noted between the healthy and the abnormal side. Readings were normal in patients with typical thyrotoxic Graves' disease. The compressibility was markedly lowered, however, in thyrotropic malignant exophthalmos. (15 figures, 5 tables, 22 references)

Gunter K. von Noorden.

Perez, E. **Intraorbital foreign bodies.** Arch. chil. de oftal. **15**:113-116, July-Dec., 1958.

The author presents the case history of a patient who had severe facial lacerations and a ruptured left globe. Surgical exploration did not reveal the point of rupture of the globe and enucleation had not been authorized and the wounds were sutured. The following day the right eye showed marked chemosis and radiographic studies revealed the presence of a knife blade in both orbits. The left eye was enucleated and a knife blade, 9 cm. long, was removed from the orbits. The right eye showed no loss of visual acuity and was not inflamed after this procedure. (3 figures)

Walter Mayer.

Sasso, B. **Primary sarcoma of the orbit.** Boll. d'ocul. **37**:675-681, Sept., 1958.

The author presents a case of a primary sarcoma of the orbit in a man of 84 years. The essential picture was that of a huge ulcerated mass which protruded from the left orbit. X rays revealed no involvement of the paranasal sinuses or of the cranial bones. No systemic metastasis could be found and therefore the author performed an exenteration of the orbit followed by electrocoagulation. On microscopic examination the lesion was found to be a fusocellular sarcoma. (7 figures, 9 references)

Joseph E. Alfano.

Schwab, F. **Further experiences with polystan implants as a means to socket formation after enucleation.** Klin. Monatsbl. f. Augenh. **135**:82-91, 1959.

Polystan is a plastic highly-polymerized derivative of ethylene. Polystan implants were used in 170 cases. Healing without complications resulted in over 95 percent of these patients. In three eyes the implant had to be removed. The cause of this complication was purulent inflammation of the socket rather than the nature of the material. Excellent tissue compatibility and a rapid uncomplicated postoperative course in almost all cases, shortened the duration of postoperative absolute bed rest and extends the scope of indications for enucleations considerably. (3 figures, 1 table, 10 references)

Gunter K. von Noorden.

15

EYELIDS, LACRIMAL APPARATUS

Fanta, H. **The place of free skin grafts in plastic surgery of the eyelids.** Ophthalmologica **137**:334-340, May, 1959.

Free whole-thickness skin grafts from the upper lid are well suited for the repair of small or medium-sized defects in the skin of the lower lids, particularly near the inner canthus. (5 figures, 5 references)

Peter C. Kronfeld.

Jacobs, H. B. **Symptomatic epiphora.** Brit. J. Ophth. **43**:415-434, July, 1959.

Blocked nasolacrimal duct is the diagnosis most frequently given as the cause of epiphora but in many cases it is actually not the causative factor. Anatomic studies have revealed great variation in the structure of the lacrimal duct system and Duke-Elder has suggested that there is a familial predisposition to tearing and

to constrictions in the ducts. In determining the cause of the epiphora it is urged that the history and physical examination be thorough and complete and that several tests be done routinely; these tests are: bacteriologic smears, dye test, Schirmer's test, dynamometric estimation of the strength of the orbicularis oculi, faradism test of the orbicularis, syringing of the system, pressure syringing, and measurement of the intercanthal distance. Despite all these tests, there will be many patients in whom the cause remains obscure.

There are two main groups of causes aside from those of mechanical obstruction of the ducts; these include a large group of cases which remained undiagnosed and a second large group of patients who were found to have a low-grade congestion and edema of the mucous membrane of the conjunctiva and of the entire lacrimal tract. The latter condition was called nasolacrimal catarrh. Symptomatic and conservative treatment of this condition resulted in a cure in many cases. (10 references) Morris Kaplan.

Kanzanjian, V. H. and Roopenian, A. **The repair of full thickness eyelid defects with special reference to malignant lesions.** Plast. & Reconst. Surg. **24**:262-270, Sept., 1959.

If there is any tension upon closing of the defect, a horizontal incision extended laterally from the outer canthus, mobilizing the skin and freeing the tarsus from the external canthal ligament, will give relaxation and allow the lateral segment of the lid to be easily advanced medially. At the lateral canthus the conjunctiva is sutured to the skin to form a new canthus. Repair of larger defects at the midsection of the lid differs from that used for smaller ones only in that greater relaxation of the skin, tarsus, and conjunctiva is required to shift medially the lateral segment of the lid to close the gap. This is done by extending the horizontal incision farther laterally at the external canthus and undermining the conjunctiva freely in the outer canthal region. To relieve the tension another incision is made laterally from the base of the defect parallel to the outer canthal incision. After a moderate amount of undermining with a blunt instrument the flap thus outlined is advanced forward and sutured. If greater relaxation is required to advance the flap, both incisions may be joined laterally to create an "island flap," the blood supply of which comes from beneath the flap. If there is insufficient mucosa, a rectangular mucosal flap may be transferred from the upper eyelid.

The Landolt-Hughes operation with modifications to suit the individual case has been quite satisfactory in the restoration of the entire upper or lower lid. An occasional complication is cicatricial contraction of the lid margin with abrasion of the cornea by the eyelashes; so the authors recommend that the hair follicles must be destroyed by electrolysis. They recommend that when the lower canaliculus has been sacrificed a special Toti-Mosher operation be done to connect the nasal cavity with the medial canthus and that this be kept open by passing a No. 2 nylon suture in through the opening thus made into the nose and out through the nostril where it is tied with the end above. The authors think that if a loop is made and moved up and down by the patient and kept in position long enough, permanent drainage can be established. They plead for adequate resection of a malignant lesion. (7 figures) Alston Callahan.

Krause, U. **A study by paper electrophoresis of human tear proteins in normal and pathologic conditions.** Acta. ophth. Suppl. 53, 1959.

Samples from 29 normal subjects and 52 patients with various diseases were investigated by paper electrophoresis and the total proteins were determined with

Folin's reagent. Six fractions were isolated; one moved more slowly than serum albumin, one corresponded with alpha 2, one approached beta. Another one showed no correspondence with any serum fraction and yet another one showed the same mobility as gamma. The fraction containing lysozyme travelled to the cathode. The difference in mobility indicates that the proteins of the tears and the serum are different substances. Considerable differences between tears and serum were also recorded in the absolute and relative sizes of the fractions in the normal material. Pathologic processes in the eye caused significant qualitative changes in the protein pattern and a significant increase in the total proteins. In monocular diseases no statistical difference was observed between absolute and relative sizes of the fractions of the two eyes; this was not true in every individual case. Atropine therapy caused an increase in the total proteins but failed to cause a qualitative normalization of the protein composition. (12 figures, 17 tables, 100 references) John J. Stern.

Vancea, P. **Transparent cyst of the lid border.** Ophthalmologica **137**:233-238, April, 1959.

The cyst was located in the anterior (skin-orbicularis) layer of the lower lid border, close to but not connected with the lower canaliculus. It had developed within the course of one year without noticeable antecedents. Histologically the cyst was found to be analogous to a gland of Moll. (7 figures, 7 references)

Peter C. Kronfeld.

Vancea, P. and Balan, N. **Bilateral sclerosing tuberculosis of the lacrimal glands.** Ophthalmologica **137**:313-320, May, 1959.

The lacrimal glands of a 21-year-old girl were the sites of symmetrical, hard, slightly tender tumors which had developed during a period of a few months. Aside from a strongly positive tuberculin reaction, all routine tests and examinations were negative. The tumors were excised in toto and found to be made up of 1. microscopic nodes with epitheloid-cell centers and lymphocytic peripheries, and 2. heavy strands of connective tissue crisscrossing the well encapsulated tumor. The centers of some of the nodules showed caseation. No bacilli were found in sections. The normal glandular structure was almost completely destroyed. The results of two animal inoculations were negative. The postoperative course was uneventful. The cosmetic result apparently was very good. No mention is made of lacrimal deficiency resulting from the extirpation of the lacrimal glands. (5 figures, 14 references)

Peter C. Kronfeld.

16
TUMORS

Oksala, A. **Echogram in melanoma of the choroid.** Brit. J. Ophth. **43**:408-414, July, 1959.

The echogram is the graph of ultrasonic waves and has been used as a diagnostic means in intrabulbar tumors since 1956. Diagnosis of melanoma of the choroid is very difficult and all too often must await its confirmation at enucleation. It has been determined that this tumor can be diagnosed with certainty by the echogram even when the tumor measures only 2 to 3 mm. in height. In this report two such diagnoses are described, one of which was of a melanoma 4 to 5 mm. in height and the other of a choroidal tumor which could not be diagnosed before it had grown to a height of 10 mm.

The instrument has been used frequently for two years with satisfactory results and the graph that it produces

demonstrates not only the height of the tumor but its width and the size of the retinal detachment as well. The resultant picture indicates the presence of the vitreous and of the lens also. Similar pictures also result from the presence of benign retinal tumors and there is as yet no means of distinguishing them from choroidal neoplasms. (4 figures, 4 references) Morris Kaplan.

Wells, A. L. **Precancerous melanosis.** Tr. Ophth. Soc. U. Kingdom **78**:165-169, 1958.

The author, a general pathologist, discusses various nevoid and melanomatous states of the conjunctiva as logical counterparts of dermatologic lesions. In a slide of precancerous melanosis he describes the diffuse proliferation of typical clear cells in the basal areas and the presence of numerous collections of pigment granules working to the surface and calls it lentigo or junctional nevus. He has found it difficult to assess the theory that malignant melanosis arising from mucous surfaces tends to be more malignant than that arising from the skin. He agrees with Ashton who advocates calling precancerous and cancerous melanosis intra-epithelial melanoma. Beulah Cushman.

17

INJURIES

Ambrosio, A. and D'Esposito, M. **Endobulbar foreign bodies. X-ray diagnosis and treatment.** Arch. di ottal. **63**:253-276, May-June, 1959.

From the results in 38 cases of endocular foreign body, the authors conclude that localization by means of the 9 millimeter corneal ring with X rays in the two primary directions is the most satisfactory. This method of Dufour was compared to five different physiologic methods and nine different geometric methods of localization. A table shows the expected radius of the globe at the equator for various degrees of ametropia and for various corneal diameters. (2 tables, 4 figures, 7 references) Paul W. Miles.

Bonaccorsi, A. **Extraction of foreign body from the deep corneal tissue or the anterior chamber.** Rassegna ital. d'ottal. **28**:March-April, 1959.

A free opening of the anterior chamber by a limbal incision with a Graefe knife is recommended by the author. If the foreign body is imbedded deeply in the cornea it may be removed by magnet or forceps. Especially when the foreign body has fallen into the angle of the anterior chamber, the free incision aids greatly in its removal. E. M. Blake.

Garzino, A. **Traumatic luxation of the globe and lesion of the optic pathways.** Rassegna ital. d'ottal. **28**:62-66, Jan.-Feb., 1959.

Injury of the optic pathway with traumatic evulsion of the globe is a rare condition. Four other cases are reported in the literature. In the author's patient a temporal hemianopsia of the remaining eye developed as a result of injury of the chiasm. In previously reported cases delayed pallor of the opposite optic disc and evidence of edema of the nervehead appeared. Severe traction of the optic nerve accounts for this lesion. E. M. Blake.

Hopping, W. **Lesions caused by close-range shots with gas pistols.** Klin. Monatsbl. f. Augenh. **135**:270-272, 1959.

During the last 30 months, 20 patients with such injuries were seen. The lesions ranged from bland conjunctival irritation with lacrimation, to destruction of the globe and severe laceration of the lids. The treatment is symptomatic. Restricted sale of these dangerous weapons is demanded. (5 references)

Gunter K. von Noorden.

Hurd, D. P. **Lime burns of the external eye.** Tr. Ophth. Soc. U. Kingdom **78**:267-273, 1958.

The most important treatment is the removal of the foreign material at the earliest possible moment and with utmost thoroughness with immediate and prolonged irrigation. The fornices should be examined and brushed clean of any particles with camel hair brushes moistened with liquid paraffin. Facial block may be necessary. Application of cortone ointment inhibits vascularization of the cornea and reduces the possibility of symblepharon. Beulah Cushman.

Kanagasundaram, C. R. **Repair of perforating injury with a scleral graft.** Brit. J. Ophth. **43**:440-441, July, 1959.

A young man received a 5 mm. penetrating tear of the sclera about 4 mm. from the limbus on the nasal side. The prolapsed ciliary body was replaced and the tear sutured directly with silk but ten days later the wound reopened and was similarly sutured only to burst open again. From a donor eye a strip of sclera 6 by 12 mm. was removed to a depth of two thirds of the sclera and sutured directly over a prepared area about the wound with 6/0 chromic gut. The eye healed rapidly and six weeks later was well healed with a clear vitreous and an unaided vision of 6/6. It had not changed a year later. (4 references)

Morris Kaplan.

Palich-Szanto, O. **A review of the Soviet literature pertaining to eye injuries during World War II.** Ophthalmologica **137**:341-352, May, 1959.

Only a few of the highlights of this review can be mentioned here. Early definitive care of the injured soldier by teams including at least one ophthalmologist was recognized as the most important principle in the treatment of eye injuries. Appositional suturing of corneal wounds gave better results than their repair by conjunctivoplasty. Intraocular injections of penicillin became routine in the care of perforating injuries.

Exact preoperative localization of an intraocular foreign body and the transcleral method of extraction contributed to a more favorable outcome of perforating injuries as compared to prewar statistics. Unfortunately, a good many of the intraocular foreign bodies during World War II were nonmagnetic. A characteristic feature of World War II was the high percentage of perforating injuries sustained by children who happened to be playing in areas from which unexploded ammunition or mines had not been completely removed. Bogdanowitsch consistently found changes in the spinal fluid (lymphocytosis and high globulin content) associated with sympathetic ophthalmia, but the total number of cases of sympathetic ophthalmia seems to have been small.

Peter C. Kronfeld

Tiburtius, H. **Eye injuries from tear gas cartridges and blank cartridges.** Klin. Monatsbl. f. Augenh. **135**:113-118, 1959.

Seventeen cases of tear gas injuries and four injuries caused by blank cartridges were treated between 1954 and 1959. Initial treatment consisted of thorough cleansing of conjunctiva and cornea, removal of foreign particles, the use of priscoline subconjunctivally or as ointment and mydriatics, bed rest, and bandage. While visual recovery occurred in most cases, two eyes with tear gas injuries developed leukoma and became practically blind. The author conducted shooting tests with both types of ammunition, which led to the conclusion that neither of these weapons are without danger to the eye and that their sale should be restricted. (1 figure, 19 references)

Gunter K. von Noorden.

18

SYSTEMIC DISEASE AND PARASITES

Baliña, L. M., Noussitou, F. and Muzzio, J. C. **Periarteritis nodosa with early ocular lesions.** Arch. oftal. Buenos Aires **33**:103-108, June, 1959.

The case of a 12-year-old boy is reported who had had attacks of recurrent bilateral plastic iridocyclitis for a year and a half, and in whom the complete picture of periarteritis nodosa developed subsequently. The ocular disturbance led to cataract formation and to intractable secondary glaucoma. ACTH and cortisone administration resulted only in transitory amelioration. The diagnosis was confirmed through the pathologic examination of biopsy material. (3 figures, 15 references)

A. Urrets-Zavalia, Jr.

Grislain, J. and Bezri, A. **Hypocalcemia with tetany and cataract complicating a case of nephrosis treated with steroids.** Ophthalmologica **137**:293-306, May, 1959.

A six-year-old French girl with lipoid nephrosis was first treated with thyroid extract and a high protein diet. This regime was maintained for two years without a significant change in the patient's condition. In full realization of the risks entailed, the patient was placed on steroids and improved to the point of being able to attend school (after having been bedridden during most of the pre-steroid period of treatment). After about six months of steroid therapy the symptoms of tetany came to the fore, accompanied by slowly progressive cataracts. Hypocalcemia was established as the cause of the visual and neurological symptoms. The addition of calcium and vitamin D to the patient's diet brought the tetany under control. Additional AT10 therapy effected a partial regression of the cataract. The authors stressed the dangers of prolonged steroid therapy and the importance of close observation of the calcium balance of the patient. (3 figures, 17 references)

Peter C. Kronfeld.

Paufique, L. and Royer, J. **The ocular signs of dysproteinemia.** Ann. d'ocul. **192**: 721-735, Oct., 1959.

Dysproteinemia occurs secondarily in diseases such as multiple myeloma and lupus erythematosus, and primarily in such diseases as macroglobulinemia and essential cryoglobulinemia. All these diseases have eye signs and in some of them the ocular findings are pathognomonic.

In the conjunctiva one may see a slowing of the blood flow with the application of ice to the closed lids for five minutes. Occasional minute hemorrhages are seen in the iris. The most marked changes are seen in the fundus. These consist of dilated, tortuous veins and scattered hemorrhages which are usually deep and in the periphery; rarely are they preretinal. The fundus itself is not cyanotic, but rather pale. Exudates are seen occasionally. This picture is also seen in the leukemias and in polycythemia vera. (4 figures, 32 references) David Shoch.

Pickering, G. W. **The influence of vascular changes in progressive failure of vision.** Tr. Ophth. Soc. U. Kingdom **78**: 295-303, 1958.

Narrowing or occlusion of the carotid artery may be the cause of many cerebral catastrophies that often are ascribed to local arterial thrombosis or hemorrhage. Episodic to sudden complete loss of vision was found without other signs in the central nervous system in two cases reported by the author. Carotid angiography demonstrated marked kinking and narrowing of the origin of the internal carotid artery. Large atheromatosis plaques and clots were removed from the internal carotid artery. One patient was made free of symptoms although the vi-

sion was not improved. It is suggested that patients in whom occlusion of the central retinal artery is suspected be investigated as to the state of the main vessels to the brain. Beulah Cushman.

19

CONGENITAL DEFORMITIES, HEREDITY

Caliglione, G. and Bonoccorsi, A. **An unusual oculo-facial malformation.** Rassegna ital. d'ottal. **28**:181-196, May-June, 1959.

After a review of the principal craniorbitofacial dysostoses the author describes a patient with this syndrome, a 23-year-old man with abnormality of the orbitofacial area. He resembles the patients described by Franceschetti and Strief. The parents of the patient were blood relatives. There were no skeletal and morphological abnormalities except hypoplasia of the mandibular symphysis and obliquity of the palpebral rim. There was also a thinning of the sclera, luxation of the lens, atrophy of a segment of the iris, and a cherry-red spot at the macula. The profile shows a parrot-like nose, arched palate, and prognathism. (5 figures) E. M. Blake.

Vanden Bosch, J. **A new syndrome in three generations of a Dutch family.** Ophthalmologica **137**:422-423, June, 1959.

The syndrome consists of mental deficiency, choroidermia with a high degree of myopia, horizontal nystagmus and an abnormal electroretinogram, in addition to a number of other somatic anomalies. Peter C. Kronfeld.

Winkelman, J. E. and Horsten, G. P. M. **Congenital blindness in the presence of a normal fundus.** Ophthalmologica **137**:423-425, June, 1959.

The condition of congenital blindness with normal fundus was present in two children, brother and sister, whose only other detectable anomaly was a herringbone pattern of the nails. Mentally the children were perfectly normal. Their father had congenital night blindness, again with normal fundus. The genetic study, apparently, could not be carried any further. Peter C. Kronfeld.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Jeandelize, P. **The "Annales d'oculistique et de gynecologie" and the "Journal d'oculistique, de medecine et de chirurgie pratiques."** Ann. d'ocul. **192**:592-595, Aug., 1959.

The author states that in 1852 a journal was published in Metz called "Revue des hopitaux civils de Metz" and subtitled "Journal d'oculistique, de medecine et de chirurgie pratiques." Thirteen issues appeared which may be found in one volume in the library of the city of Metz. David Shoch.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

ANNOUNCEMENTS

OHIO POSTGRADUATE CONFERENCE

The Department of Ophthalmology, Ohio State University School of Medicine, announces an ophthalmology postgraduate conference to be held at the Ohio State Union Building, Columbus, Ohio, March 7th and 8th. On Monday, March 7th, Dr. William H. Havener will discuss "Experiences with the light coagulator"; Dr. Rocko Fasanella, New Haven, Connecticut, "Alpha chymotrypsin"; Dr. Paul Boeder, Iowa City, "Anisometropic prescriptions"; Dr. Phillips Thygeson, San Jose, California, "Ocular changes in dermatologic disease"; Dr. Torrence A. Makley, Columbus, Ohio, "Ocular fungus infections"; Dr. Boeder, "Magnification and telescopic lenses." There will be a dinner meeting with the Columbus Academy of Eye, Ear, Nose and Throat after which Dr. Fasanella will speak on "Nasolacrimal surgery."

On Tuesday March 8th, Dr. Thygeson will speak on "Keratitis" and "Conjunctivitis." Dr. Makley will discuss "Modern therapy of sympathetic ophthalmia"; Dr. Fasanella, "Complications of cataract surgery"; Dr. Boeder, "Accommodation-convergence relationships"; Dr. Havener, "Service for you."

The registration fee for the conference is $20.00. Further inquiries should be addressed to Dr. William H. Havener, Department of Ophthalmology, University Hospital, Columbus 10, Ohio.

WASHINGTON HOSPITAL CENTER

Continuing the series of Saturday morning lectures, the Training and Education Committee of the Department of Ophthalmology, Washington Hospital Center, 110 Irving Street, N.W., Washington 10, D.C., announces that on March 5th the subject for discussion will be "Injuries," with Dr. John H. Lodge speaking on "Nonperforating injuries," Dr. John R. Weimer, "Perforating injuries," and Dr. William D. Foote, "Intraocular foreign bodies."

"Retinal diseases" will be the subject of the lectures on March 12th, 19th, and 26th.

On March 12th, Dr. George N. Wise will speak on "Arterior and arteriolosclerosis," "Vascular retinopathies (diabetic and renal)," "Thrombosis and embolism."

On March 19th, Dr. John W. McTigue will speak on "Eales' disease, Coats' disease, and hemangiomatosis retinae"; Dr. Henry L. Bastien, "Senile degenerations and treatment"; Dr. Harry M. McAllister, "Lesions of the posterior pole and differential diagnosis."

On March 26th, Dr. Marshall M. Parks will speak on "Infantile and juvenile macular degenerations"; Dr. Nicholas G. Pistolas, "Retrolental fibroplasia and anoxia"; Dr. Dan G. Albert, "Retinoblastoma."

OKLAHOMA CITY ACADEMY

The sixth annual spring meeting of Oklahoma City Academy of Ophthalmology and Otolaryngology with the Postgraduate Department of the University of Oklahoma Medical Center will be held on March 3rd and 4th. Ophthalmologist guest speakers will be: Victor A. Byrnes, M.D., St. Petersburg, Florida, and Daniel Snydacker, M.D., Chicago, Ill. For further information write Dr. E. Norris Robertson, Jr., 301 N.W. 12th Street, Oklahoma City, Oklahoma.

AMBLYOPIA POSTGRADUATE COURSES

Dr. Curt Cüppers, Giessen, Germany, will give an intensive course in "The treatment of amblyopia, theory, instrument demonstration and practical application," from March 7th to 18th. The course is limited to 20 ophthalmologists. Fee: $100.00. In addition, Dr. Cüppers will give a series of three lectures on "Introduction to the therapy of amblyopia by the help of the after-image method," on March 21st and 23rd. Fee: $25.00. For registration, please apply to: Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3, New York.

XIX INTERNATIONAL CONGRESS

All ophthalmologists are cordially invited to attend the XIX International Congress of Ophthalmology in Delhi, December 3 to 7, 1962. This will be the first congress to be held in Asia.

There will be two main subjects and four symposia. The subjects will be announced as soon as they are chosen by the International Council in 1960. There will be about 50 free papers. The free papers will be scrutinized by a committee of the International Council in addition to the National Council. The International Association for the Prevention of Blindness and the International Organization against Trachoma will hold meetings during the congress. The two languages chosen by the International Council are English and French.

The registration fees are: (1) for members from the ophthalmological societies affiliated to the International Federation: 150 Indian rupees; (2) for members from nonfederated countries: 165

Indian rupees; (3) for associated members (wives and children accompanying the members): 50 Indian rupees; (4) for scientific members: 50 Indian rupees, without participation in social functions.

All correspondence and requests for information should be sent to the secretary-general, Dr. Y. K. C. Pandit, Bombay Mutual Building, Sir Pherozeshah Mehta Road, Bombay 1, India.

Ophthalmic plastic surgery

A three-week intensive course in ophthalmic plastic surgery will be conducted in New York April 25th to May 14th. The course will consist of lectures, sessions in doctors' offices, preliminary and follow-up cases that are operated on during the time of the course, moving picture demonstrations of various ophthalmic plastic procedures, observation and assistance at the operating table on actual surgical cases, cadaver work and lectures and demonstrations, ancillary subjects such as photography, pathology and X-ray and radiation.

The course will be limited to eight students and will be given at the New York Eye and Ear Infirmary, Manhattan Eye, Ear and Throat Hospital and the Hempstead General Hospital under the auspices of the Institute of the Americas. The fee will be $250.00.

Anyone interested should contact the Registrar of the Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary or any of the following: Dr. Wendell L. Hughes, Hempstead, New York; Dr. Byron C. Smith, New York City; Dr. J. Gordon Cole, New York City.

Miscellaneous

Fight for Sight awards

The National Council to Combat Blindness, Inc., New York, announces the grants-in-aid, clinical service projects, predoctoral and postdoctoral research fellowships, and summer student fellowships approved at the June, 1959, meeting of the Scientific Advisory Committee.

For the *Grants-in-aid:* Francis H. Adler, William C. Frayer, Hospital of the University of Pennsylvania, Philadelphia, "Study of the factors involved in the proliferation of the retinal pigment epithelium in disease," $1,000; Edgar Auerbach, Hadassah University and Medical School, Jerusalem, "Impaired vision and its connection with light (color) sense," $1,500; Endre A. Balazs, Retina Foundation, Boston; "Studies on the hyaluronic acid formation in the vitreous body," $4,000; Gilbert Baum, New York University Postgraduate Medical School, New York, "A comparison of the acoustic properties of benign and malignant ocular tissues," $5,000; Robert Brunish, University of Virginia School of Medicine, Charlotte, "Characterization of the ophthalmotrophic hormone," $6,900; Charles J. Campbell, Columbia University College of Physicians and Surgeons, New York, "The determination of adaptometric thresholds of various regions of the retina in normal and pathologic subjects and the relation of the thresholds to the clinical appearance of the fundus," $4,155; Paul A. Cibis, Washington University School of Medicine, St. Louis, "Histopathology of the eye with oblique illumination," $6,512; Robert M. Day, Columbia University, College of Physicians and Surgeons, New York, "Exophthalmos inhibiting factor in human serum," $1,200; Anthony Donn, Columbia University College of Physicians and Surgeons, New York, "Factors influencing the active transport of sodium into the corneal stroma," $1,500; Levon K. Garron, Helenor Campbell Foerster, Francis I. Proctor Foundation, University of California, San Francisco, "Special histopathologic study of endogenous uveitis," $4,500; Frederick G. Germuth, Jr., and Lawrence B. Senterfit, Charlotte Memorial Hospital, Charlotte, North Carolina, "Studies on antigen-antibody reaction in the avascular cornea," $5,000; Calvin Hanna, University of Vermont, Burlington, Vermont, "Studies on cataract formation," $3,254; C. W. Hargens, The Franklin Institute of the State of Pennsylvania, Philadelphia, "Development, exploration and application of a glaucoma detector based on induced vibrations of the eyeball," $3,000; Ray Hepner, University of Maryland School of Medicine, Baltimore, "The effects of maternal hyperoxemia on the intrauterine development of the eye," $1,750; Gilbert Iser, University of Illinois, Chicago, "Role of the a-wave in clinical electroretinography," $3,000; Jerry Hart Jacobson, New York Eye and Ear Infirmary, New York, "Behavioral studies of higher level vision in monkeys," $5,000; Walter Kornblueth, Hadassah University Hospital, Jerusalem, "Metabolism of orbital fat," $3,800; Abraham L. Kornzweig, Home for Aged and Infirm Hebrews of New York, "The eye in old age: A clinical and pathologic study," $1,250; Albert P. Ley, Washington University School of Medicine, St. Louis, "Histology of zonulolysis with alpha chymotrypsin," $4,975; Louise G. Lovekin, Yale University, New Haven, Connecticut, "Physiological reaction to glass implantation in tissues," $750; Cecil P. Luck, University College of East Africa, Kampala, Uganda, Africa, "Comparative ophthalmology of mammals, with special reference to primates," $4,500; William R. Sistrom, Harvard University, Cambridge, Massachusetts, "The role of carotene pigments in the structure and function of the chromatophores of photosynthetic bacteria," $5,000; George K. Smelser, Columbia University, College of Physicians and Surgeons, New York, "Investigations on the pathogenesis of experimental exophthalmos," $2,400; Jun Tsutsui, Okayama Rosai Hospital, Okayamashi, Japan, "Immunochemical studies of corneal protein in homo- and hetero-corneal grafts," $1,400; Jerome J. Wolken, University of Pittsburgh Medical Center, Pittsburgh, "Photoreceptor structures," $3,132.

A special grant was made for payment to specialized personnel for the development of a scientific protocol for the investigation of 11-cis vitamin A as a therapy for retinitis pigmentosa and one

which will provide future investigators with a standard procedure for the evaluation of therapies purported to be beneficial in the treatment of this disease, $4,500.

Grants for the *clinical services projects to:* Dan M. Gordon, New York Hospital-Cornell Medical Center, New York, "For the maintenance and improvement of low vision clinic: Application of visual aids in patients with subnormal vision," $2,250; Harry M. Holtz, Newark Beth Israel Hospital, Newark, New Jersey, "To provide instruments and equipment for tonography in glaucoma and suspected glaucoma," $1,000; Ralph E. Kirsch, Mt. Sinai Hospital, Miami Beach, Florida, "Purchase of equipment to assist in the establishment of an eye clinic," $2,500.

The *predoctoral and postdoctoral research fellowships* granted were: Leslie A. Bard, Johns Hopkins Hospital, Baltimore, "Serum proteins in diabetes and diabetic retinopathy," $2,000; Philip W. Brandt, Columbia University College of Physicians and Surgeons, New York, "A study of solute movement across the endothelial-like cells and epithelial cells lining the anterior segment of the eye," $4,400; Tavisak Chulavachana, Tulane University School of Medicine, New Orleans, "Studies regarding ocular staphylococcal infections," $4,800; Bengt Olof Hedbys, Retina Foundation, Boston, "Studies on corneal dehydration and experimental keratoplasty," $5,000; Ake Sigurd Holmberg, Washington University School of Medicine, St. Louis, "Ultrastructure of the ciliary epithelium and the trabecula," $2,500; Arthur B. Leith, University of London, London, "Measurement of episcleral and aqueous vein pressures in open angle glaucoma," $2,400; Maria Th. Matton-Van Leuven, Duke University School of Medicine, Durham, North Carolina, "Comparative studies, by tissue culture and grafting of viability of animal and human corneas, frozen at various temperatures," $3,600; Johannes W. Rohen, Washington University School of Medicine, St. Louis, "Experimental studies on the histology of the trabecular meshwork," $5,000; Tsugihiko Tokunga, State University of Iowa, University Hospitals, Iowa City, "Cytological study in electron microscopy on radiation cataract: Study on incipient opacities of experimental cataracts," $1,200; Isamu Tsukahara, Columbia University College of Physicians and Surgeons, New York, "Ophthalmic pathology," $2,500.

The *summer student fellowships* granted were: George W. Applegate, Johns Hopkins University School of Medicine, Baltimore, "Experimental production of ocular tumors and surface epithelial downgrowths in the animal eye," $600; William J. Bean, Tulane University School of Medicine, New Orleans, "Re-examination of the physiology of aqueous humor kinetics: Application of newly developed techniques on the study of aqueous humor kinetics to ophthalmic pharmacology," $600; John Bergland, Johns Hopkins University, School of Medicine, Baltimore, "Investigations in ocular hypersensitivity," $600; Christopher D. Burda, Tulane University School of Medicine, New Orleans, "Experimental fungal keratitis in rats," $600; John M. Burket, State University of Iowa College of Medicine, Iowa City, "Histological studies of the iris with especial consideration of the dilator fibers: Comparison of animals and man using various techniques," $400; Rosa Mae Christy, University of California Medical Center, San Francisco, "Histochemical study of the distribution of acid mucopolysaccharides, carbohydrates, and lipids in the anterior segment of the rat eye," $600; Martin R. Feller, State University of New York, Downstate Medical Center, New York, "Temperature gradients in the rabbit eye," $550; Ernest W. Franklin, III, Charlotte Memorial Hospital, Charlotte, North Carolina, "Studies of antigen-antibody reactions in the avascular cornea," $600; David R. Hopkins, Retina Foundation, Boston, "Interaction between collagen and other macromolecules in collagen gels," $400; Howard M. I. Leibowitz, Johns Hopkins University School of Medicine, Baltimore, "Investigations in ocular hypersensitivity, $600; Henry S. Metz, State University of New York, Downstate Medical Center, New York, "Determination of the proteolytic activity of the lens of the eye," $600; James E. O'Brien, University of Vermont College of Medicine, Burlington, Vermont, "Intracellular biochemical changes in the gamma ray treated eye," $600; John L. Overby, Tulane University School of Medicine, New Orleans, "Immunochemical analysis of corneal proteins: I. Comparison of various animal species," $600; Michael S. Schafrank, State University of New York, Downstate Medical Center, New York, "Changes in the pH of the aqueous of the enucleated rabbit eye with time," $600; Ernest Eun-Ho Shin, Eye and Ear Hospital University of Pittsburgh, Pittsburgh, "Physicochemical mechanism of energetics in photoreception, with main emphasis on energy transfer: Energy transfer in the photoreceptor of Euglena gracilis," $600; James F. Stiles, State University of Iowa College of Medicine, Iowa City, "The penetration of radio labeled cortisone and hydrocortisone in normal eyes with certain pathologic abnormalities," $600; Shigemi Sugiki, Washington University School of Medicine, St. Louis, "Tissue culture of the ciliary body epithelium: Effects of cyanide, anoxia, carbonic anhydrase inhibitors, etc.," $600; Saeko Watanabe, Okayama Rosai Hospital, Japan, "Electrophoretic analysis of corneal protein: Comparative analysis of corneal protein fraction in different kinds of animal species," $250; Paul Witkovsky, University of California Los Angeles, "Attempt to correlate electroretinographic responses with retinal development using the embryonic chick: To begin with a systematic examination (histologically) of the developing retina at various time intervals," $600; Philip H. Zweifach, Cornell University Medical College, New York, "Alterations in intraocular pressure induced by blood osmolol changes," $600.

Bunts Educational Institute

The Frank E. Bunts Educational Institute affiliated with the Cleveland Clinic Foundation, Cleveland, Ohio, recently sponsored a postgraduate course on "Newer developments in ophthalmology." Guest speakers were Dr. Arthur H. Keeney, Louisville, Kentucky; Dr. James T. Mayer, Cleveland; Dr. Edmund B. Spaeth, Philadelphia; and Dr. Richard C. Tröutman, Brooklyn. From the faculty of the Bunts Institute were: Dr. Robin Anderson, Department of Plastic Surgery; Dr. John D. Battle, Jr., Department of Hematology; Dr. William A. Hawk, Department of Pathology; Dr. Roscoe J. Kennedy, Department of Ophthalmology; Dr. Charles L. Leedham, Director of Education; Dr. James E. Nousek, Jr., Department of Ophthalmology; and Dr. Carl E. Wasmuth, Department of Anesthesiology.

Course for contact lens technicians

Ohio State University, Department of Ophthalmology, Columbus, Ohio, is giving a six-month course for contact lens technicians, starting January 1, 1960. Preceptor type of training, being given in the contact lens clinic, includes the fitting and adjustment of lenses on patients. Students attend basic science lectures with orthoptic students.

Societies

Brooklyn meeting

Dr. Bernard Schwartz was chairman for the discussion on "Current problems in glaucoma diagnosis and therapy," the subject considered at the 154th regular meeting of the Brooklyn Ophthalmological Society. Dr. Martin Feuerman spoke on "Echothiophate (phospholine iodide) in the treatment of glaucoma"; Dr. Schwartz on "Some problems in the diagnosis and treatment of angle-closure in glaucoma"; Dr. Robert Jampel, "Field changes in glaucoma"; and Dr. Miles Galin, "Uses of urea for the control of intraocular hypertension."

Dallas Academy

At the January 5th meeting of the Dallas Academy of Ophthalmology and Otolaryngology Dr. Sam E. Roberts, Kansas City, Missouri, spoke on "Neurovascular dysfunction of the eighth nerve." At the February 5th meeting, Dr. Raymond N. Berke, Hackensack, New Jersey, will discuss "Surgical correction of ptosis."

Southern Medical Association

At the meeting of the Southern Medical Association in Atlanta, Georgia, the following officers were elected for the Section of Ophthalmology and Otolaryngology for the coming year: Chairman, Dr. George M. Haik, New Orleans; chairman-elect, Dr. Mercer G. Lynch, New Orleans; vice-chairman, Dr. Bernard J. McMahon, Clayton, Missouri; secretary, Dr. Albert C. Esposito, Huntington, West Virginia.

The following papers on Ophthalmology were presented and discussed:

"Surgical management of congenital glaucoma," George Meyer, S. D. McPherson, Jr., and G. T. Kiffney, Jr., Durham, North Carolina, discussed by Alston Callahan, Birmingham; "Tonography in office practice," Joseph Derivaux, Birmingham, discussed by Lynne S. Gamble, Greenville, Mississippi; "Use of alpha chymotrypsin in cataract surgery," Ben H. Jenkins, Newnan, Georgia, discussed by Morgan B. Raiford, Atlanta; "Acute glaucoma following extraocular surgery despite definitive ocular preventive measures." S. B. Forbes, Tampa, Florida, discussed by Albert C. Esposito, Huntington, West Virginia.

"Surgery of the inferior oblique muscle," George G. Ellis, New Orleans, discussed by George M. Haik, New Orleans; "Entopic phenomena and the aging eye," Albert E. Meisenbach, Jr., Dallas, Texas, and Albert E. Meisenbach, Sr., Saint Louis, Missouri, discussed by J. Jack Stokes, Atlanta; "The ophthalmologist and problems of contact lenses," Frederick E. Hasty, Coral Gables, Florida, discussed by Kenneth E. Whitmer, Miami, Florida.

The next meeting of the Section will be held in Saint Louis, Missouri, from October 31 to November 3, 1960. Those interested in participating should write to the secretary of the Section, Dr. Albert C. Esposito.

II. Afro-Asian congress

The program for the II. Afro-Asian Congress of Ophthalmology to be held in Tunis includes:

Reports on "Viral disease of the eye," and "Keratoplasty." Symposiums on "Therapeutics of trachoma," "Vernal catarrh," and "Pterygium." Free papers will be presented. At the conclusion of the sessions there will be a two-day sight-seeing tour.

For further information write to: Dr. Ridha M'Rad, Centre Ophtalmolgique, Tunis.

Dallas Southern Clinical Society

Dr. Arthur G. DeVoe and Dr. Herman Elwyn, both of New York, will be ophthalmic guest speakers at the 29th annual spring clinical conference of the Dallas Southern Clinical Society, to be held at the Statler-Hilton, Dallas, Texas, March 21, 22, and 23.

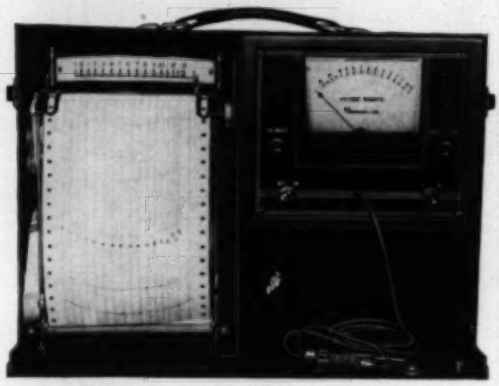
Dr. DeVoe will speak on "Ophthalmic plastic surgery," "Diseases of the cornea," and "Congenital defects." The subjects Dr. Elwyn will present are "Heredodegenerations of the retina," "Fundus changes in benign essential hypertension," and "Arteriospastic retinopathy."

Personal

Dr. Albert M. Potts has been appointed professor of ophthalmology in the Department of Surgery and director of research in ophthalmology at the University of Chicago.

Dr. Potts has been a member of the faculty of Western Reserve University, Cleveland, since 1948. He was associate professor of ophthalmic research from 1954 to 1959. A biochemist and a specialist in toxicology of the eye and in electrophysiology, Dr. Potts will conduct research in these areas at the University of Chicago, in addition to his teaching and clinical duties.

THE ONLY COMPLETE TONOGRAPHY UNIT



Electric Tonometer and Recorder combined in a single portable unit!

Developed and built exclusively by V. Mueller. This portable Tonography Unit brings a long-needed, major contribution to modern tonographic research. The Tonometer is greatly improved, more rugged, less subject to interference, and easier to read. Specially adapted large graph recording device.

OP-Mueller Electronic Tonographer TR. For 110 volts, 60 cycles, AC. .....Each, $895.00

Improved Mueller Electronic Tonometer or Recording Unit EA are also available separately.

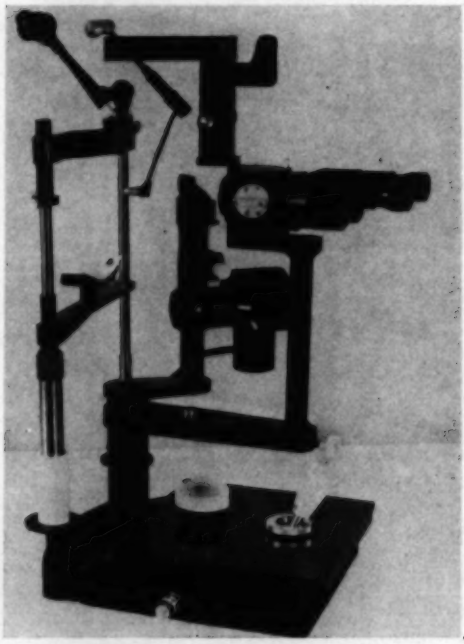
Write for the New, Complete Brochure on the Electronic Tonometer and Tonographer

V. MUELLER & CO.

Fine Surgical Instruments and Hospital Equipment

330 S. Honore St., Chicago 12, Ill. · Dallas · Houston · Los Angeles · Rochester, Minn.

Armamentarium



THE GOLDMANN SLIT LAMP APLANATION TONOMETER ALSO FOR THE ZEISS SLIT LAMP

ADVANTAGES:

- Great accuracy of measurement
- Direct reading of measured values in MM Hg
- Rigidity of the eye can be disregarded since the small displacement of volume does not increase the intraocular pressure by more than about 2%
- Tonometry becomes a routine examination within the usual Slit Lamp Microscopy
- The patient remains seated during the examination
- Precision Swiss workmanship

Reprints of Dr. Th. Schmidt's (associate of Prof. H. Goldmann, Bern, Switzerland) recent lecture on Aplanation Tonometry delivered in this country, are available from us. No charge.

IMMEDIATE DELIVERY FROM OUR STOCK

ALFRED P. POLL

Ophthalmological Instruments of Top Quality

40 WEST 55th STREET, NEW YORK 19, N.Y.

Patients generally report noticeable relief from light disturbances.

One in a series of professional evaluations of Therminon Lenses.
Name and address on request.

Therminon LENSES

THERMINON LENS CORPORATION • 63RD AT UNIVERSITY • DES MOINES, IOWA

BERENS PHYSICIANS FLASH LIGHT with INTERCHANGEABLE TIPS for DIAGNOSIS AND SURGERY

Plastic tips are shielded allowing light to emerge only at the working point.

Tips available are:
"A" Globe retractor for Retinal-Detachment Surgery.
"B" Posterior Globe Illuminator.
"C" Anterior Illuminator.
"D" Focal Illuminator.
"E" Cobalt Blue for use with Fluorescein in Contact Lens fitting and Corneal examination.
"F" Multi-Spot, Six combinations of Red, Green and White for Color and Binocular Vision tests, Retinal Response in Cataract and Fixation.

Available in three sets:

Complete set of Light and six tips less batteries	$35.00
Retinal Detachment set, Light and tips "A,B,C,D"	$22.50
Diagnostic set, Light and tips "C,D,E,F"	$22.50
Long Life Mercury Batteries, each	$ 1.00
Tip Adapter for Welch Allyn Transilluminator	$ 2.75

Available at all Optical and Surgical Suppliers
Manufactured by

225 Cadwalader Avenue **R. O. GULDEN** Philadelphia 17, Penna.

Schiotz Tonometer Standardization—Repair—Maintenance service.

It's NEW

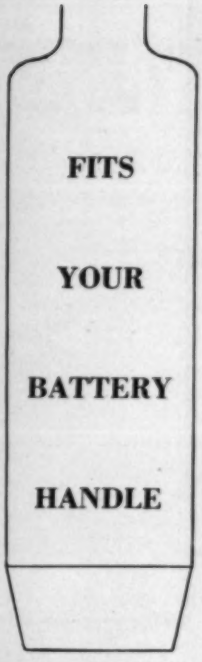
The RHEO-TRAN unit
Illumination Control

NO BATTERIES

Send for literature

OPHTHALMIC OPTICIANS
Wholesale Rx Service
Since 1920

Main Office **109 N. Wabash, at Washington**
Chicago, Illinois



In contact lenses

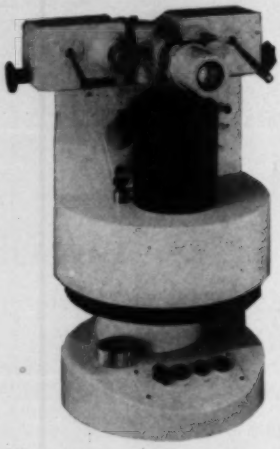
Concentra® Corneal Lenses
Lacrilens® Molded Plastic Lenses
Solutionless Contact Lenses
Plastic Contact Trial Sets
Plastic Spherical Contact Lenses
Prism Contact Lenses
Cylindrical Contact Lenses
Plastic Microscopy Lenses
Plastic Gonioscopic Lenses
Colored Contact Lenses
Tinted Contact Lenses
Wetting Solutions
Plastic Molding Shells
Molding Equipment
Radius Gauges
Thickness Gauges
Textbooks

IT'S OBRIG
FOR EVERYTHING IN SIGHT

A pioneer in plastic contact lens development and manufacture, Obrig Laboratories maintains leadership in the contact lens field through continuous, imaginative research. In experience, facilities and range of products and services, Obrig will not be surpassed. The list of Obrig products is a growing one; to its customers Obrig offers consultation and assistance in problem fitting cases. In contact lenses – it's Obrig for everything in sight.

Obrig Laboratories, Inc.

75 East 55th Street, New York 22, N.Y. · PLaza 8-0960
Florida: P. O. Box 791, Sarasota
Foreign Branches: Montreal, Canada
Johannesburg, South Africa
San Jose, Costa Rica
Caracas, Venezuela



Pleoptophor
After Bangerter

A new instrument for the treatment of amblyopia, combining the best known up-to-date methods, like the dazzling-stimulating method of Bangerter and the after-image method according to Cueppers. This is an important step forward in the training of central fixation.

This instrument will be demonstrated by the Swiss ophthalmologist, Dr. A. Graemiger, assistant to Dr. Bangerter, in our booth at the academy meeting.

Ophthalmological Instruments of Top Quality

ALFRED P. POLL

40 WEST 55TH STREET, NEW YORK 19, N.Y.

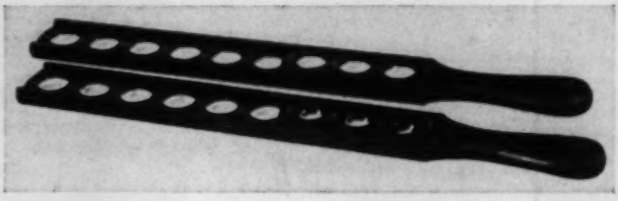
MATALENE

SURGICAL INSTRUMENTS CO., INC.

GRAND CENTRAL PALACE BUILDING • 125 EAST 46TH ST., N. Y. 17, N. Y.

Successors to E. B. Meyrowitz Surgical Instruments Co., Inc.

NEW MODEL
SKIASCOPIC RACKS



These racks are used in retinoscopy, being held by the patient and moved up or down according to the doctor's directions. Contact with the patient's face is prevented by metal rims.

This method of retinoscopy is more convenient and much quicker than the method of using trial lenses in a trial frame.

Each of the racks, both plus and minus, contains 1, 2, 3, 4, 5 and 6 D lenses one inch in diameter. A supplementary slide on one side carries .25, .50 and .75 D lenses and a supplementary slide on the other side carries a 6 D lens. Every lens power from .25 D to 12.75 D in both plus and minus is obtainable.

Price, for set of two, $89.50

with

DEGEST®

ocular decongestant

Degest® immediately relieves corneal edema and inflammation of ocular epithelial tissues which may result from excessive contact lens wearing. These conditions, if not treated, subside slowly.

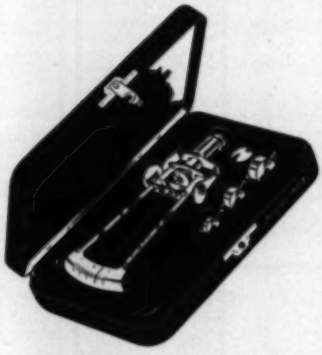
Degest® speeds the subsidence . . . soothes, refreshes, clears ocular tissues.

Ingredients: Phenylephrine hydrochloride 0.2% in a mildly hypertonic vehicle, benzalkonium chloride 0.01% and sodium bisulfite 0.1%, as preservatives.

Degest® is supplied as a sterile, hypertonic, neutral solution in 15 cc. dropper bottles.

Manufactured by **BARNES-HIND** Ophthalmic Products, Inc., 895 Kifer Road, Sunnyvale, California . . . designers and manufacturers of Barnes-Hind Wetting Solution, Barnes-Hind Soquette Solution, and Barnes-Hind Minims Fluorescein Cotton Tip.

New



IMPROVED SCHIOTZ TONOMETER*

Designed by R. O. GULDEN *Manufactured by* PILLING

This new tonometer conforms exactly to the most recent specifications set by the Committee on Standardization of Tonometers of the American Academy of Ophthalmology and Otolaryngology. It features:

- **Perfect balance of instrument and weights.**
- **Friction-free movement.**
- **Ventilated foot plate, preventing capillary action in plunger tube.**
- **Wrap-around indicator—eliminates parallax in reading.**
- **Entire construction of stainless steel and anodized aluminum.**
- **New all plastic case—easy to clean—washable-unbreakable.**

Special brochure available on request.

Each instrument is certified by the Electrical Testing Laboratory of New York.

* Patent Pending

ORDER DIRECT FROM

GEORGE P. *PILLING* & SON CO.

3451 Walnut Street • Philadelphia

Pilling New York Office 4 - W. 56th St., N.Y. 19, N.Y.

Other Offices: Columbus, Ohio - Atlanta, Georgia - Los Angeles, Calif. **CABLE ADDRESS: Surgical - Phila.**

GREINER & MUELLER

Expert makers
of artificial human eyes

GLASS & PLASTIC

55 E. Washington St. . . . Chicago 2, Ill.
Phone FR 2-4449
Branches at Kansas City, Mo., Detroit, Mich.
Our experts visit Milwaukee, Madison, Minneapolis, and St. Louis regularly. Serving the Middle West since 1924.

Eye making has been a family tradition with us since 1835.

For the Discriminating Eye Physician

Depend on the Services of a Guild Optician

GUILD Rx OPTICIANS

IN LYNCHBURG, VA.

A. G. JEFFERSON

Ground Floor Allied Arts Bldg.

Exclusively Optical

For vacuum-coated Sun- and Protection Lenses as well as for special coatings

contact **BALZERS**

Europe's foremost coating-manufacturer.

BALZERS Aktiengesellschaft

Balzers, Principality of Liechtenstein

It Will Pay You

to look through the advertising pages of this Journal.

We discriminate as to the quality and reliability of the advertising accepted for the

AMERICAN JOURNAL
of
OPHTHALMOLOGY

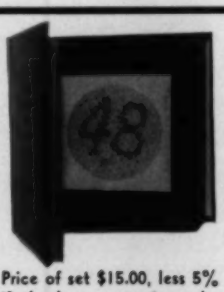
DVORINE PSEUDO-ISOCHROMATIC PLATES*

OFFER THESE EXCELLENT FEATURES

- Distinguishes the color-blind from the color-ignorant
- Classifies the color-blind according to type and severity of defect
- Special arrangement prevents malingering. Complete directions with each set

WRITE FOR FREE LITERATURE

*The most widely accepted test in the U.S. Used by Medical Examiners of the CAA, Veterans Administration and the U.S. Armed Forces.



SCIENTIFIC PUBLISHING CO.

Dept. A—2328 Eutaw Place Baltimore 17, Maryland

Price of set $15.00, less 5% if check accompanies order

CHICAGO OPHTHALMOLOGICAL SOCIETY— 1960 CLINICAL CONFERENCE

February 12 and 13, 1960 **The Drake Hotel, Chicago, Ill.**

SPEAKERS

Walter S. Atkinson, M.D.
Gilbert Baum, M.D.
James Bennett, M.D.
Paul Cibis, M.D.
Robert Hollenhorst, M.D.
Bertha A. Klien, M.D.
Peter Kronfeld, M.D.
Oscar Sugar, M.D.
Isaac Tassman, M.D.

SUBJECTS

Symposium: "Retinal Disorders"
Ophthalmodynamometry in Intracranial Vascular Disease
Observations of Cataract Surgery
Ultrasonography in Clinical Ophthalmology
Photocoagulation of Iris and Retina
Surgical Treatment of Total Xerophthalmia
Other subject to be announced

Fee: $45.00 (Includes Round Table Luncheons and Dinner following Gifford Lecture)

Registrar: MRS. MARY E. RYAN
1150 North Lorel Avenue, Chicago 51, Illinois

THE SIXTEENTH ANNUAL GIFFORD MEMORIAL LECTURE

DR. WALTER S. ATKINSON, Watertown, New York
Friday, February 12, 1960, The Drake Hotel, 5:15 P.M.

The Chicago Ophthalmological Society extends an invitation to all physicians to attend the Lecture. A dinner which follows is open to physicians and their wives.

URGENT REQUEST

The Uveitis Laboratory, University of California School of Medicine, San Francisco, is vitally interested in obtaining freshly enucleated eyes from patients with all types of uveitis and other endogenous inflammations. Attempts are being made to isolate etiologic agents from these eyes.

The eyes should be placed in a sterile bottle, packaged with the history and findings, and shipped as quickly as possible. Please send specimens special delivery, collect, and mark the package "Fresh Tissue Specimen—Rush." Do not freeze or use preservatives of any kind.

A report of isolations of organisms and pathologic findings, including a slide, will be sent to the contributor. Credit will be given in any resulting publications if desired.

Telegraph collect if specimen being sent.

Send eyes to

Samuel J. Kimura, M.D., Michael J. Hogan, M.D., or Phillips Thygeson, M.D.
University of California School of Medicine
San Francisco 22

THE GILL MEMORIAL EYE, EAR AND THROAT HOSPITAL

Announces to the Profession its

THIRTY-THIRD ANNUAL SPRING CONGRESS IN OPHTHALMOLOGY AND OTOLARYNGOLOGY

April 4 through April 9, 1960

GUEST SPEAKERS

Leonard Apt, M.D. .....Philadelphia, Pennsylvania
William F. Barry, Jr., M.D. ..Durham, North Carolina
Francis B. Catlin, M.D. .....Baltimore, Maryland
James E. Crushore, M.D. .....Detroit, Michigan
John F. Daly, M.D. .....New York, New York
Edward A. Dunlap, M.D. .....New York, New York
John A. Dyer, M.D. .....Rochester, Minnesota
Ben S. Fine, M.D. .....Washington, D.C.
John R. Heller, M.D. .....Bethesda, Maryland
John W. Henderson, M.D. .....Ann Arbor, Michigan
William H. Kaufman, M.D. .....Roanoke, Virginia
Alexander McCausland, M.D. .....Roanoke, Virginia
P. Robb McDonald, M.D. ..Philadelphia, Pennsylvania
Franklin B. McKechnie, M.D. ...Richmond, Virginia
Alton Ochsner, M.D. .....New Orleans, Louisiana
Peter N. Pastore, M.D. .....Richmond, Virginia
George E. Shambaugh, Jr., M.D. ....Chicago, Illinois
Harvey E. Thorpe, M.D. ....Pittsburgh, Pennsylvania

FOR FURTHER INFORMATION WRITE:
Superintendent, P.O. Box 1789
Roanoke, Virginia

NEW YORK UNIVERSITY POST-GRADUATE MEDICAL SCHOOL

offers

OPHTHALMIC PLASTIC SURGERY
(For Specialists)

Part time, 2 to 5 p.m., February 29 through March 4, 1960. Covers the essentials of ophthalmic plastic surgery for the practicing ophthalmologist. Under the direction of Dr. Sidney A. Fox. Tuition $90

SURGERY OF THE EYE
(For Specialists)

Full time, March 28 through April 2, 1960. Includes practical work on the cadaver and operative clinics at University, Bellevue and Lenox Hill hospitals. Under the direction of Dr. Rudolf Aebli. Tuition $140

OPHTHALMOSCOPY

Part time, 9 a.m. to 12 m., April 25 through 29, 1960. Includes a study of the normal fundus, congenital anomalies, diseases of the vitreous, retina, choroid, optic nerve head, and traumatic fundus changes. Under the direction of Dr. George N. Wise. Tuition $60

HISTOPATHOLOGY

Part time, 1 to 4 p.m., April 25 through 29, 1960. Consists of lectures, demonstrations and microscopic study of exemplary material. Under the direction of Dr. A. Marvin Gillman. Tuition $100

For additional information
Office of the Associate Dean
New York University-Bellevue Medical Center
550 First Avenue · New York 16, N.Y.

UNIVERSITY OF MICHIGAN MEDICAL CENTER

Postgraduate Conference in Ophthalmology

The annual conference in Ophthalmology will be held April 25, 26 and 27, 1960, at the Rackham Graduate School Building, Ann Arbor, Michigan.

Dr. F. Bruce Fralick and Staff of the Department of Ophthalmology will conduct the conference. The following named guest lecturers will participate:

Dr. Frank D. Costenbader, Washington
Dr. Windsor S. Davies, Detroit
Dr. John E. Harris, Minneapolis
Dr. William F. Hughes, Chicago
Dr. Fred G. Blum, Madison
Dr. F. Dale Roth, St. Louis
Dr. Thomas P. Stratford, Richmond
Dr. David D. Donaldson, Boston

Applications may be addressed to the Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

AN EMPLOYMENT REGISTRY FOR SCIENTISTS

in the basic sciences appertaining to OPHTHALMOLOGY AND OTOLARYNGOLOGY has been established by the American Academy of Ophthalmology and Otolaryngology. The Registry will aid in the placement of candidates completing training who desire academic and investigative positions, and in the replacement of those already in such positions who desire a different position. It will also serve institutions seeking to fill such positions.

Since the Registry will be of considerable service to scientists in the fields of Ophthalmology and Otolaryngology, it will be operated by the Academy without fee or obligation.

For further information and registry forms, write to

American Academy of Ophthalmology and Otolaryngology Registry
W. L. Benedict, M.D., Executive Secretary
15 Second Street S.W., Rochester, Minn.

It Will Pay You

to look through the advertising pages of this Journal.

We discriminate as to the quality and reliability of the advertising accepted for the

AMERICAN JOURNAL
of
OPHTHALMOLOGY

PRESCRIPTION OPTICIANS

ST. LOUIS, MO.

Erker Bros. Optical Co.

908 Olive Street
518 N. Grand Boulevard
and 33 N. Central Ave., Clayton, Mo.
Prescription Opticians Since 1879

Dow Optical Co.
PRESCRIPTION SPECIALISTS
Suite 1015 30 N. Michigan Avenue
Chicago, Illinois
Phone RAndolph 6-2243-44
DEALERS IN OPHTHALMOLOGICAL EQUIPMENT

PORTLAND, ORE.

Hal. H. Moor, 315 Mayer Bldg.

Guild Optician

Oculists' prescriptions exclusively

L. M. Prince OPTICIANS
Specialists in filling ophthalmologists' prescriptions with utmost care.

Cincinnati, Ohio	4 West 4th St. 23 Garfield Pl. 411 Oak St.
Dayton, Ohio	117 S. Ludlow
Covington, Ky.	623 Scott St.
Newport, Ky.	3rd & Washington

PERFECTION, SKILL, and SERVICE SINCE 1872

"OPHTHALMIC LITERATURE"

AN ABSTRACT JOURNAL IN ENGLISH OF THE WORLD'S CURRENT LITERATURE ON OPHTHALMIC SUBJECTS

Indispensable to the busy practitioner for quick reference and timely useful information.

"Ophthalmic Literature" and Index (8 numbers) Yearly subscription—Four Guineas ($13.50 U.S.A.). Published by British Medical Association.

U.S.A. Agent

MEDICAL MARKET RESEARCH, INC.
East Washington Square,
Philadelphia 5, U.S.A.

BRITISH JOURNAL OF OPHTHALMOLOGY

Published monthly by
The British Medical Association

Annual Subscription $20.00

OPHTHALMIC LITERATURE

A comprehensive abstract of
ophthalmology and cognate literature.

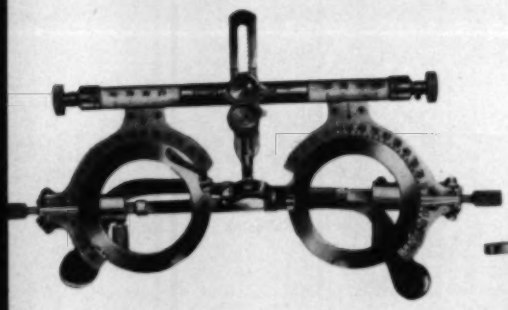
Six issues and index yearly.
Annual Subscription $13.50

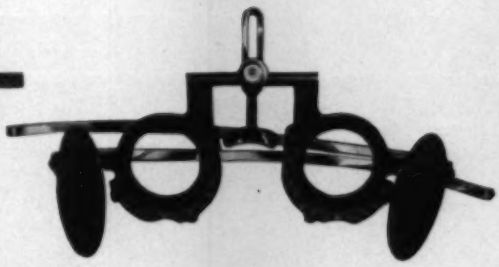
Combined annual subscription to British Journal of
Ophthalmology and Ophthalmic Literature $30.00

Subscriptions to:

MEDICAL MARKET RESEARCH INC.
East Washington Square,
Philadelphia 5, U.S.A.

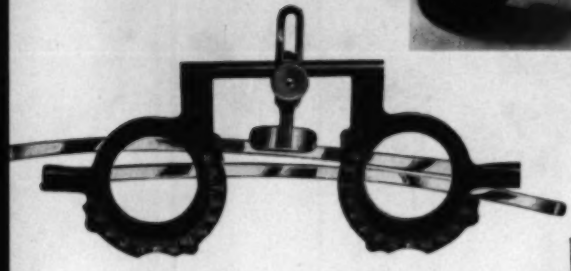
Refraction Aids

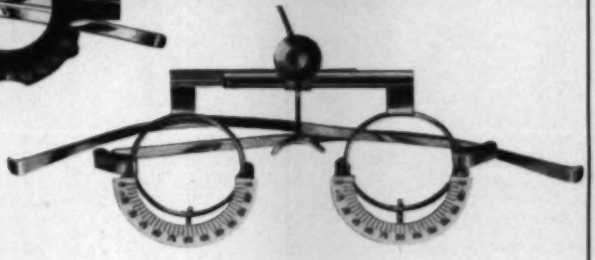




The central illustration shows a novel yet inexpensive occluder which clips on to the patient's spectacle when subjectively checking V.A. The spring-clip is polythene sleeved to protect the spectacle lens.

The surrounding illustrations feature various types of trial frames, all of which are light weight, durable and efficient.





Whatever your requirements, speedy and efficient service will attend your enquiry to KEELER OPTICAL PRODUCTS, INC., 5536 BALTIMORE AVENUE, PHILADELPHIA 43, PA. (TELEPHONES GRanite 4-5310 and KIngswood 4-0874).

KEELER OPTICAL PRODUCTS INC.

5536 Baltimore Avenue, Philadelphia 43, Pa.

Today...for those who attend to the disorders of the eyes...

Prednefrin®

ophthalmic suspension

for mild to moderate inflammatory and allergic eye disorders

PREDNEFRIN—the formula for greater effectiveness—in the topical treatment of ophthalmic inflammatory reactions, is indicated whenever the repository effect of a "solution like" suspension is desired. Prednefrin provides a unique, multi-dimensional approach for greater objective and subjective effectiveness with the anti-inflammatory action of *prednisolone 0.12%*, the decongestant effectiveness of *phenylephrine 0.12%* and the soothing, lubricating properties of *methylcellulose 0.12%*. SUPPLIED: 5 cc. plastic bottles.

Prednefrin S®

ophthalmic solution

for moderate to severe inflammatory and allergic eye disorders

PREDNEFRIN S is unexcelled for the topical treatment of the more severe ophthalmic inflammatory condition. Potent anti-inflammatory action *(prednisolone alcohol 0.2%)* plus valuable decongestant action *(phenylephrine 0.12%)*. Prednefrin S, *a special solution*, assures the patient of a uniform concentration, with freedom from stinging or burning on instillation, as well as freedom from irritation, as long as therapy continues. SUPPLIED: 5 cc. plastic dropper bottles.

ALLERGAN CORPORATION

Los Angeles 17, California

APPS-1